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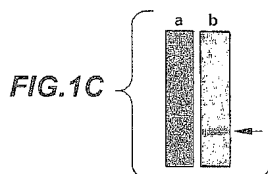
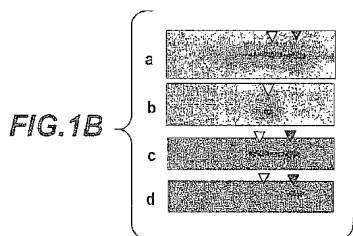
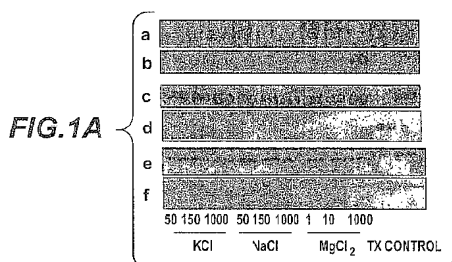
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(54) Title: TREATMENT OF LYSOSOMAL STORAGE DISEASES



(57) Abstract: Methods and compositions useful in the treatment or prevention of lysosomal storage diseases, such as Pompe's disease, Fabry's disease, Gaucher's disease, and Niemann-Pick disease, are provided. The treatment includes administering to a subject a farnesyl transferase inhibitor compound. The treatment may also include enzyme replacement therapy or gene therapy.

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TREATMENT OF LYSOSOMAL STORAGE DISEASES

Related Applications

[0001] The present invention claims priority under 35 U.S.C. § 119(e) to U.S. provisional patent application, USSN 60/894,086, filed March 9, 2007, which is incorporated herein by reference.

Field of the Invention

[0002] The present invention relates to the treatment of lysosomal storage diseases, such as Gaucher's disease, Fabry's disease, Niemann-Pick disease, and Pompe's disease.

Background of the Invention

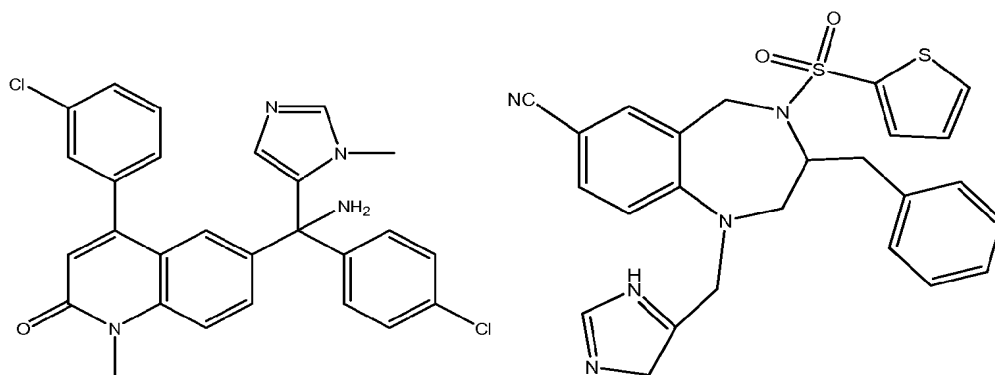
[0003] The lysosome is a cytoplasmic organelle that functions to degrade macromolecules such as proteins, polynucleotides, polysaccharides, and lipids. The lysosome encloses an acidic environment and contain enzymes which catalyze the hydrolysis of biological macromolecules. The lysosome has also been found to play a role in the uptake of molecules via endocytosis.

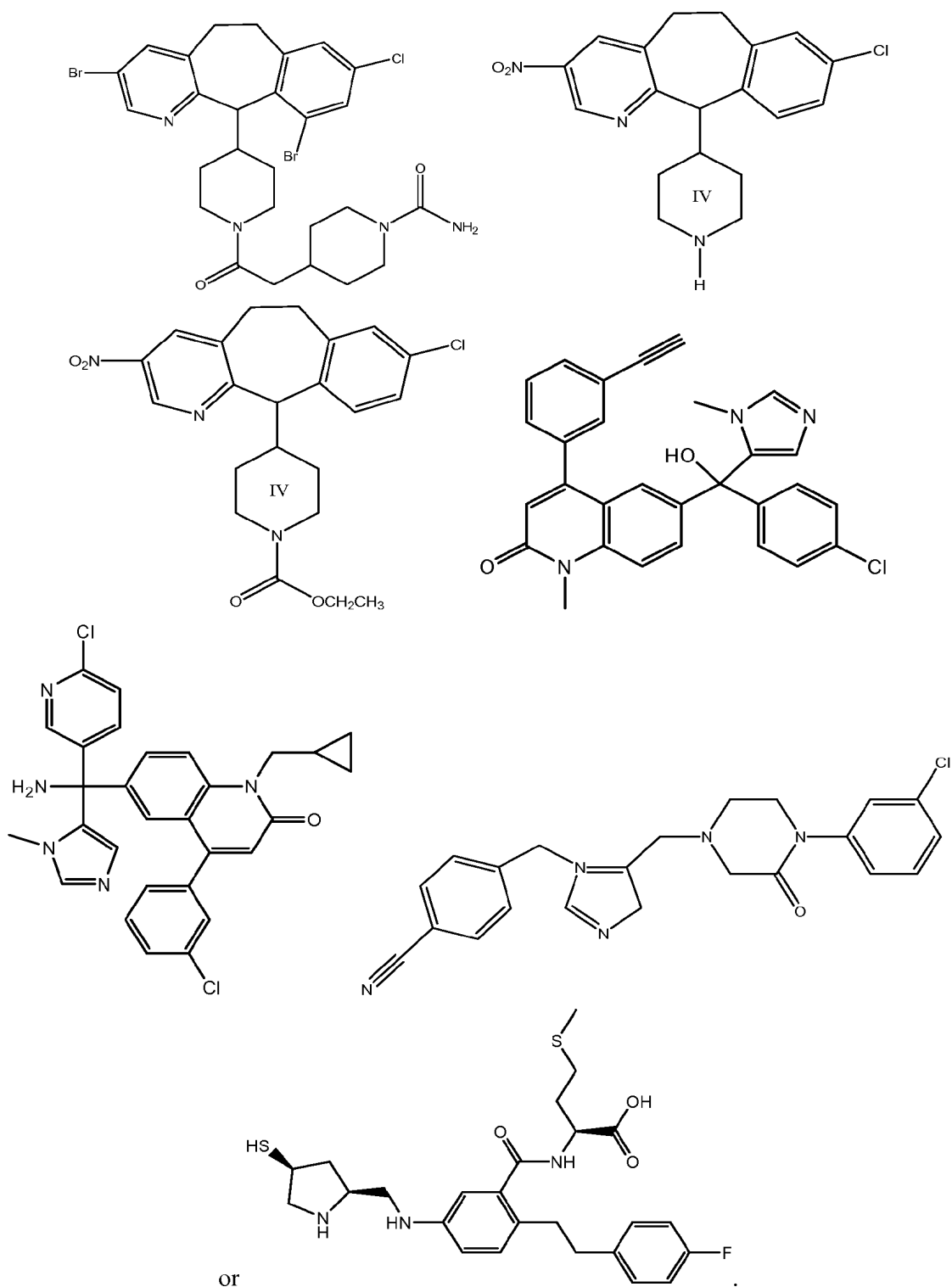
[0004] Lysosomal storage diseases occur when a lysosomal protein is deficient or mutant. In many cases, this protein is an enzyme, and abnormal deposits of the substrate of the deficient enzyme accumulate in the cell. In other cases, the deficient protein is involved in trafficking, post-translational processing, or protection or activation of a lysosomal enzyme. In still other cases, the defective protein is not an enzyme but exists in the intra-lysosomal space or spans the lysosomal membrane. The function of some of these proteins is presently unknown. There is extensive clinical and biochemical heterogeneity within the lysosomal storage diseases, which include most of the lipid storage disorders, the mucopolysaccharides, the mucopolidoses, and glycoprotein storage diseases. Currently there are over forty lysosomal storage disorders known including Niemann-Pick disease, Fabry's disease, Gaucher's disease, *etc.* The disorders are typically progressive and frequently are fatal in childhood or adolescence. Genetic counseling is important in the management of these diseases, and specific therapies such as enzyme replacement therapy are promising but expensive. Typically the care for these patients is largely symptomatic. There remains a need for additional therapies to treat these often fatal diseases.

Summary of the Invention

[0005] The present invention relates to therapeutic approaches to the treatment of lysosomal storage diseases, such as glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F, by treatment with a farnesyl transferase inhibitor.

[0006] In one aspect, the invention provides methods for treating a subject with a lysosomal storage disease by administering a therapeutically effective amount of a farnesyl transferase inhibitor or composition thereof. In certain embodiments, the farnesyl transferase inhibitor is a small molecule. In some embodiments, the farnesyl transferase inhibitor is of one of the formulae disclosed herein, or a derivative, analog, stereoisomer, isomer, solvate, polymorph, or salt thereof. Exemplary farnesyl transferase inhibitors useful in the treatment of lysosomal storage diseases include compounds of the formulae:





[0007] In another aspect, the invention provides methods for treating a subject with a lysosomal storage disease by administering both a farnesyl transferase inhibitor or

composition thereof, and a second therapeutic agent or composition thereof. The two compounds and/or compositions can be administered as a combination composition comprising both compounds. Alternatively, the two compounds can be administered separately (*e.g.*, as two different compositions) either simultaneously or sequentially as described herein. In some embodiments, a farnesyl transferase inhibitor composition includes one or more farnesyl transferase inhibitors disclosed herein, or a derivative, analog, stereoisomer, isomer, solvate, or salt thereof. In some embodiments, the second therapeutic agent may be, but is not limited to, enzyme replacement therapy or pharmacological chaperone therapy. In some embodiments, the second therapeutic agent may be related to gene therapy, in which the gene of the defective protein is replaced or altered.. In certain embodiments, the second therapeutic agent provides palliative or supportive care for the symptoms of the lysosomal storage disease. The second therapeutic agent may or may not treat the underlying lysosomal storage disease.

[0008] It should be appreciated that aspects and embodiments of the invention described herein in connection with one farnesyl transferase inhibitor may also be practiced using two or more farnesyl transferase inhibitors (*e.g.*, between 2 and 50; between 2 and 25; between 2 and 10; between 2 and 5; 2, 3, 4, 5, 6, 7, 8, or 9). Similarly, aspects and embodiments of the invention described herein in connection with one other agent also may be practiced using two or more other agents (*e.g.*, between 2 and 50; between 2 and 25; between 2 and 10; between 2 and 5; 2, 3, 4, 5, 6, 7, 8, or 9).

[0009] In another aspect, the present invention provides kits for the treatment of a lysosomal storage disease. The inventive kits include a farnesyl transferase inhibitor or a pharmaceutical composition thereof for the treatment of a lysosomal storage disease. The kits may also include other agents for treating the underlying lysosomal storage disease or symptoms thereof as described herein. The kit typically includes multiple doses of each of the farnesyl transferase inhibitor and the optional second therapeutic agent. The kit may include enough dosages of each agent for treating a subject for one week, two weeks, three weeks, one month, two months, three months, six months, or longer. The kit may also include devices for administering the agents such as a spoon, syringe, *etc.* The kit also typically includes prescribing information for the agents included in the kit.

Brief Description of the Drawing

[0010] *Figure 1* shows that UCH-L1 membrane association is regulated by its farnesylation.

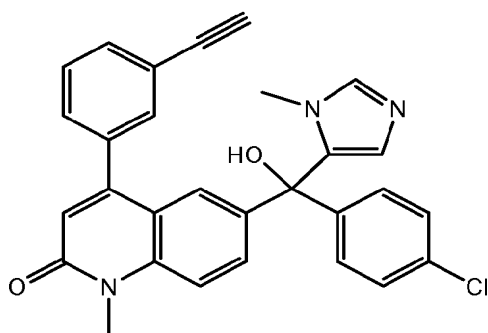
[0011] *Figure 2* shows that C220S mutation abolished the inhibitory effect of UCH-L1 WT on α -synuclein degradation.

[0012] *Figure 3* (top panel) shows LC3 immunostaining in SHSY-5Y cells treated with LNK-754 as compared to control. The bottom panel of *Figure 3* shows LC3 mRNA expression in SHSY-5Y cells treated with LNK-754, Zarnestra, and rapamycin.

Detailed Description of Certain Embodiments of the Invention

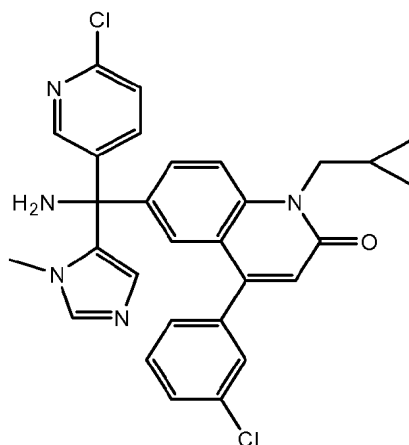
[0013] The invention provides a system for treating patients with lysosomal storage diseases. In certain embodiments, the invention includes methods of treating a subject with a lysosomal storage disease, such as glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F. In certain embodiments, the lysosomal storage disease being treated is Pompe disease. In certain embodiments, the lysosomal storage disease being treated is Fabry disease. In certain embodiments, the lysosomal storage disease being treated is Gaucher disease. In certain embodiments, the lysosomal storage disease being treated is Niemann-Pick disease. Without wishing to be bound by any particular theory or mechanism of action, the methods of the invention are useful in modulating autophagy by changing the expression of LC-3 or other autophagy-related proteins. The invention provides methods for treating a subject with a lysosomal storage disease, including the step of administering to the subject a therapeutically effective amount of a farnesyl transferase inhibitor or composition thereof. In certain embodiments, the subject is a mammal. In certain specific embodiments, the subject is a human. The human may be male or female, and the human may be at any stage of development.

[0014] In one embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:



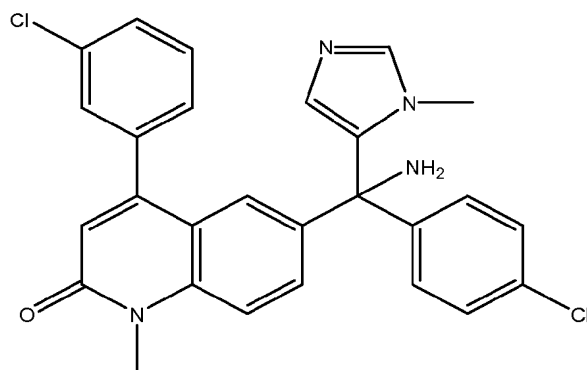
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency. In certain embodiments, the tartrate salt of the compound is administered.

[0015] In one embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:



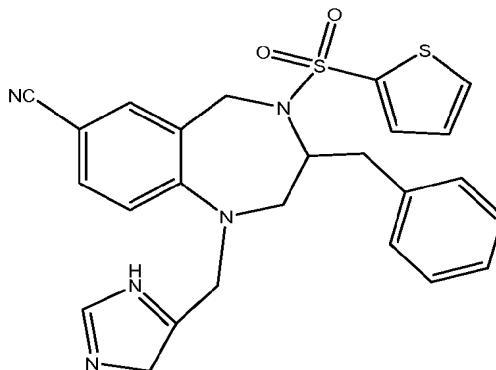
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency. In certain embodiments, a salt of the compound is administered.

[0016] In one embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:



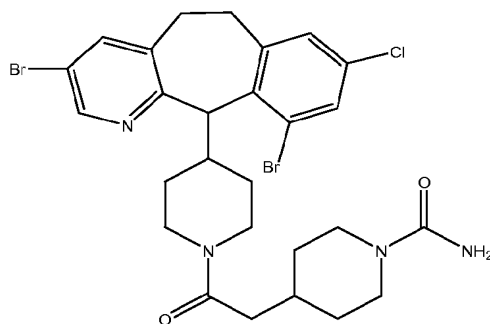
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency. In certain embodiments, a salt of the compound is administered.

[0017] In one embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:



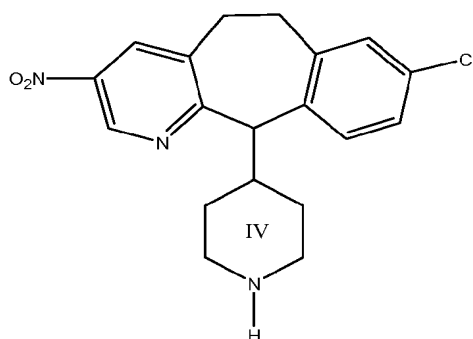
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency. In certain embodiments, a salt of the compound is administered.

[0018] In one embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:



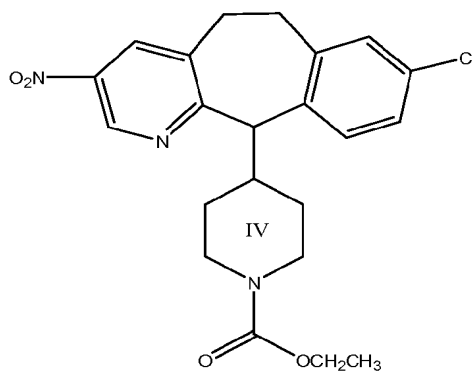
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency. In certain embodiments, a salt of the compound is administered.

[0019] In one embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:



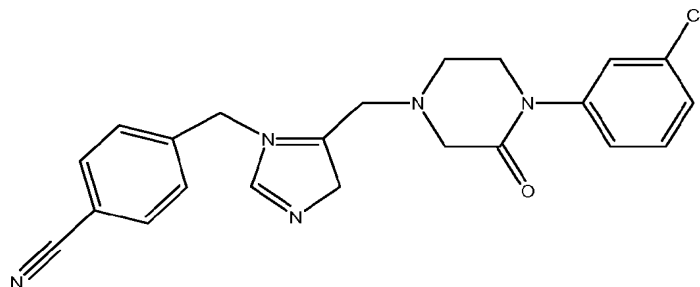
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency. In certain embodiments, a salt of the compound is administered.

[0020] In one embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:



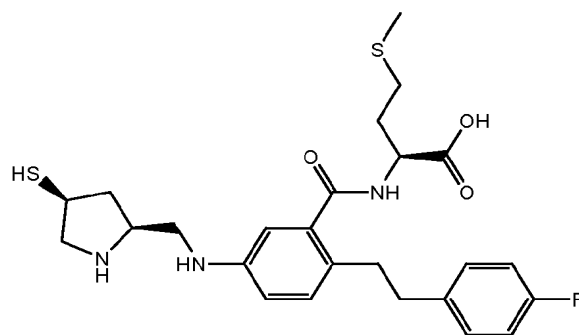
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency. In certain embodiments, a salt of the compound is administered.

[0021] In one embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:



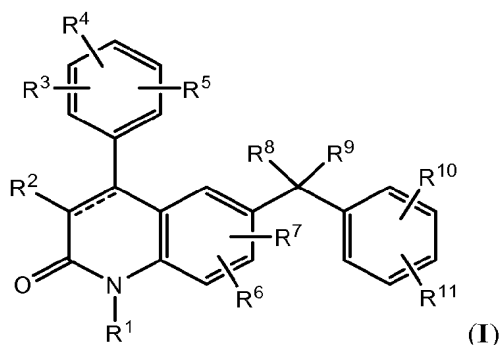
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency. In certain embodiments, a salt of the compound is administered.

[0022] In one embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:



or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency. In certain embodiments, a salt of the compound is administered.

[0023] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (I):



wherein

the dashed line indicates that the bond between C-3 and C-4 of the quinolin-2-one ring is a single or double bond;

R^1 is selected from H, C_1 - C_{10} alkyl, $-(CR^{13}R^{14})_qC(O)R^{12}$, $-(CR^{13}R^{14})_qC(O)OR^{15}$, $-(CR^{13}R^{14})_qOR^{12}$, $-(CR^{13}R^{14})_qSO_2R^{15}$, $-(CR^{13}R^{14})_t(C_3$ - C_{10} cycloalkyl), $-(CR^{13}R^{14})_t(C_6$ - C_{10} aryl), and $-(CR^{13}R^{14})_t(4$ -10 membered heterocyclic), wherein t is an integer from 0 to 5 and q is an integer from 1 to 5, said cycloalkyl, aryl and heterocyclic R^1 groups are optionally fused to a C_6 - C_{10} aryl group, a C_5 - C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; and the foregoing R^1 groups, except H but including any optional fused rings referred to above, are optionally substituted by one to four R^6 groups;

R^2 is halo, cyano, $-C(O)OR^{15}$, or a group selected from the substituents provided in the definition of R^{12} ;

each R^3 , R^4 , R^5 , R^6 , and R^7 is independently selected from H, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, halo, cyano, nitro, mercapto, trifluoromethyl, trifluoromethoxy, azido, $-OR^{12}$, $-C(O)R^{12}$, $-C(O)OR^{12}$, $-NR^{13}C(O)OR^{15}$, $-OC(O)R^{12}$, $-NR^{13}SO_2R^{15}$, $-SO_2NR^{12}R^{13}$, $-NR^{13}C(O)R^{12}$, $-C(O)NR^{12}R^{13}$, $-NR^{12}R^{13}$, $-CH=NOR^{12}$, $-S(O)_jR^{12}$ wherein j is an integer from 0 to 2, $-(CR^{13}R^{14})_t(C_6$ - C_{10} aryl), $-(CR^{13}R^{14})_t(4$ -10 membered heterocyclic), $-(CR^{13}R^{14})_t(C_3$ - C_{10} cycloalkyl), and $-(CR^{13}R^{14})_tC\equiv CR^{16}$, and wherein in the foregoing R^3 , R^4 , R^5 , R^6 , and R^7 groups t is an integer from 0 to 5; the cycloalkyl, aryl and heterocyclic moieties of the foregoing groups are optionally fused to a C_6 - C_{10} aryl group, a C_5 - C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; and said alkyl, alkenyl, cycloalkyl, aryl and heterocyclic groups are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-NR^{13}SO_2R^{15}$, $-SO_2NR^{12}R^{13}$, $-C(O)R^{12}$, $-C(O)OR^{12}$, $-OC(O)R^{12}$, $-NR^{13}C(O)OR^{15}$, $-NR^{13}C(O)R^{12}$, $-C(O)NR^{12}R^{13}$, $-NR^{12}R^{13}$, $-OR^{12}$, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, $-(CR^{13}R^{14})_t(C_6$ - C_{10} aryl), and $-(CR^{13}R^{14})_t(4$ -10 membered heterocyclic), wherein t is an integer from 0 to 5;

R^8 is H, $-OR^{12}$, $-NR^{12}R^{13}$, $-NR^{12}C(O)R^{13}$, cyano, $-C(O)OR^{13}$, $-SR^{12}$, $-(CR^{13}R^{14})_t$ (4-10 membered heterocyclic), wherein t is an integer from 0 to 5, or C_1 - C_6 alkyl, wherein said heterocyclic and alkyl moieties are optionally substituted by 1 to 3 R^6 substituents;

R^9 is $-(CR^{13}R^{14})_t$ (imidazolyl) wherein t is an integer from 0 to 5 and said imidazolyl moiety is optionally substituted by one or two R^6 substituents;

each R^{10} and R^{11} is independently selected from the substituents provided in the definition of R^6 ;

each R^{12} is independently selected from H, C_1 - C_{10} alkyl, $-(CR^{13}R^{14})_t$ (C_3 - C_{10} cycloalkyl), $-(CR^{13}R^{14})_t$ (C_6 - C_{10} aryl), and $-(CR^{13}R^{14})_t$ (4-10 membered heterocyclic), wherein t is an integer from 0 to 5; said cycloalkyl, aryl and heterocyclic R^{12} groups are optionally fused to a C_6 - C_{10} aryl group, a C_5 - C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; and the foregoing R^{12} substituents, except H, are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NR^{13}C(O)R^{14}$, $-C(O)NR^{13}R^{14}$, $-NR^{13}R^{14}$, hydroxy, C_1 - C_6 alkyl, and C_1 - C_6 alkoxy;

each R^{13} and R^{14} is independently H or C_1 - C_6 alkyl, and where R^{13} and R^{14} are as $-(CR^{13}R^{14})_q$ or $(CR^{13}R^{14})_t$ each is independently defined for each iteration of q or t in excess of 1;

R^{15} is selected from the substituents provided in the definition of R^{12} except R^{15} is not H;

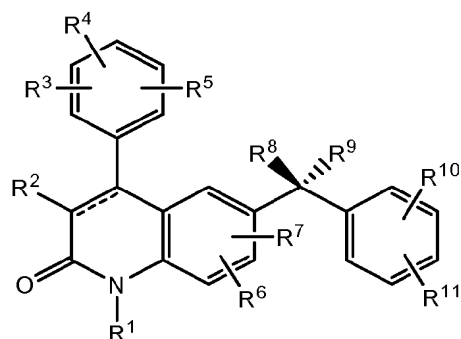
R^{16} is selected from the list of substituents provided in the definition of R^{12} and $-\text{Si}R^{17}R^{18}R^{19}$;

R^{17} , R^{18} , and R^{19} are each independently selected from the substituents provided in the definition of R^{12} except R^{17} , R^{18} , and R^{19} are not H; and

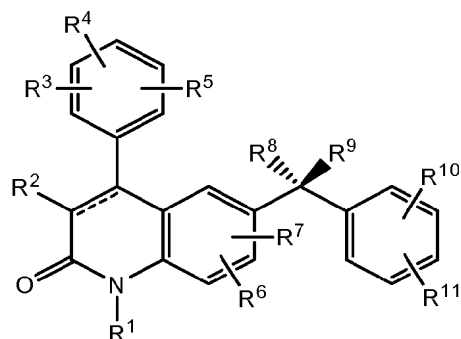
provided that at least one of R^3 , R^4 , and R^5 is $-(CR^{13}R^{14})_tC\equiv CR^{16}$ wherein t is an integer from 0 to 5 and R^{13} , R^{14} , and R^{16} are as defined above;

or a derivative, analog, stereoisomer, isomer, solvate, or salt form thereof, at a therapeutically effective dose and frequency. In certain embodiments, a racemate is used in the invention. In other embodiments, an enantiomerically pure compound is used. In other embodiments, an enantiomerically enriched mixture is used (e.g., 70%, 75%, 80%, 90%, 95%, 98%, 99% of one enantiomer).

[0024] For certain compounds of formula I, the stereochemistry is defined as follows:



[0025] For other compounds of formula I, the stereochemistry is defined as follows:



[0026] In certain classes of compounds of formula I, the dashed line represents one bond of a double bond between C-3 and C-4 of the quinolin-2-one ring.

[0027] In other classes of compounds of formula I, R¹ is H or C₁-C₆ alkyl. In certain compounds useful in the invention, R¹ is H, methyl, ethyl, *iso*-propyl, or *n*-propyl. In certain particular compounds, R¹ is methyl.

[0028] In other classes of compounds of formula I, R² is H, halo, or C₁-C₆ alkyl. In certain compounds, R² is H.

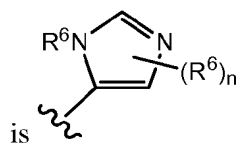
[0029] In yet other classes of compounds of formula I, one of R³, R⁴, and R⁵ is –(CR¹³R¹⁴)_tC≡CR¹⁶, wherein t is an integer from 0 to 5, inclusive, and R¹³, R¹⁴, and R¹⁶ are as defined above; and the other two of R³, R⁴, and R⁵ are H. In other compounds, one of R³, R⁴, and R⁵ is –C≡CH. In yet other compounds, one of R³, R⁴, and R⁵ is –C≡CH; and the other two of R³, R⁴, and R⁵ are H.

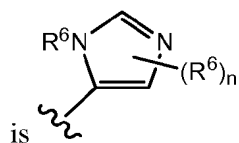
[0030] In other classes of the compounds of formula I, R⁶ is H.

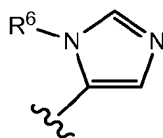
[0031] In other classes of the compounds of formula I, R⁷ is H.

[0032] In yet other classes of the compounds of formula I, R⁸ is H, –OR¹², or –NR¹²R¹³, wherein R¹² and R¹³ are as defined above. R⁸ is hydroxy or amino. In other compounds, R⁸ is hydroxy. In yet other compounds, R⁸ is amino.

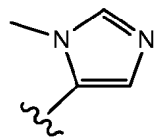
[0033] In certain classes of the compounds of formula **I**, R^9 is an imidazolyl moiety, optionally substituted with one or two R^6 substituents, wherein R^6 is defined as above. In certain compounds, R^9 is an imidazolyl moiety substituted with one R^6 substituents, wherein R^6 is defined as above. In certain compounds, R^9 is an imidazolyl moiety substituted with one R^6 substituents, wherein R^6 is C_1 - C_6 alkyl, preferably methyl. In certain compounds, R^9

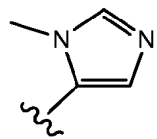


is , wherein R^6 is as defined above and t is an integer between 0 and 2,



inclusive. In other compounds, R^9 is , wherein R^6 is as defined above. In other



compounds, R^9 is .

[0034] In certain classes of the compounds of formula **I**, R^{10} is H, C_1 - C_{10} alkyl, halo, cyano, nitro, or amino. In certain compounds, R^{10} is halo, preferably chloro or fluoro. In certain particular compounds, R^{10} is chloro. In certain compounds, at least one of R^{10} and R^{11} is H.

[0035] In certain classes of the compounds of formula **I**, R^{11} is H, C_1 - C_{10} alkyl, halo, cyano, nitro, or amino. In certain compounds, R^{11} is halo, preferably chloro or fluoro. In certain particular compounds, R^{11} is chloro.

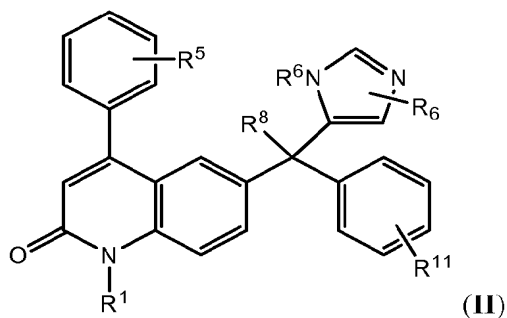
[0036] Certain compounds of formula **I** include those wherein R^1 is H, C_1 - C_6 alkyl, or cyclopropylmethyl; R^2 is H; R^3 is $-C\equiv CR^{16}$; and R^8 is $-NR^{12}R^{13}$, $-OR^{12}$, or a heterocyclic group selected from triazolyl, imidazolyl, pyrazolyl, and piperidinyl, wherein said heterocyclic group is optionally substituted by an R^6 group. Other compounds of formula **I** include those wherein R^9 is imidazolyl optionally substituted by C_1 - C_6 alkyl; R^8 is hydroxy, amino, or triazolyl; and R^4 , R^5 , R^{10} and R^{11} are each independently selected from H and halo.

[0037] Other compounds of formula **I** include those wherein R^1 is $-(CR^{13}R^{14})_t(C_3-C_{10}$ cycloalkyl), wherein t is an integer from 0 to 3; R^2 is H; R^3 is $-C\equiv CR^{16}$; and R^8 is $-NR^{12}R^{13}$, $-OR^{12}$, or a heterocyclic group selected from triazolyl, imidazolyl, pyrazolyl, and piperidinyl, wherein said heterocyclic group is optionally substituted by an R^6 group. Yet other compounds of formula **I** include those wherein R^9 is imidazolyl, optionally substituted by C_1 -

C₆ alkyl; R⁸ is hydroxy, amino, or triazolyl; R⁴, R⁵, R¹⁰ and R¹¹ are each independently selected from H and halo; and R¹ is cyclopropylmethyl.

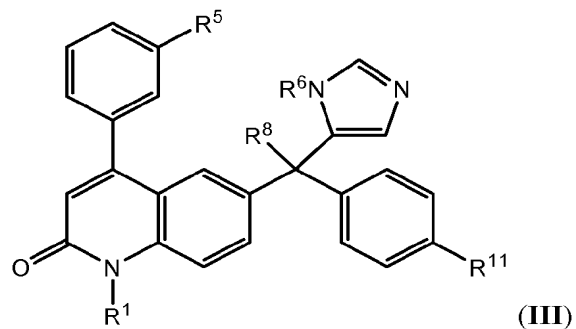
[0038] Other compounds of formula I include those wherein R³ is ethynyl and the other substituents are as defined above. Other compounds of formula I include those wherein R³ is -C≡CR¹⁶. For certain compounds, R¹⁶ is H. For other compounds, R¹⁶ is -SiR¹⁷R¹⁸R¹⁹. For other compounds, R¹⁶ is C₁-C₆ alkyl.

[0039] Compounds useful in the present invention include compounds of the formula (II):



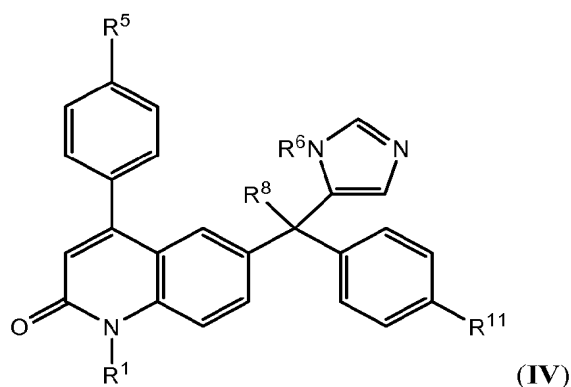
wherein R¹, R⁵, R⁶, R⁸, and R¹¹ are defined as above.

[0040] Compounds useful in the present invention also include compounds of the formula (III):



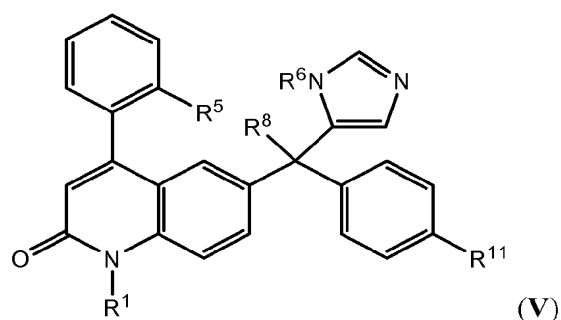
wherein R¹, R⁵, R⁶, R⁸, and R¹¹ are defined as above.

[0041] Compounds useful in the present invention include compounds of the formula (IV):



wherein R^1 , R^5 , R^6 , R^8 , and R^{11} are defined as above.

[0042] Compounds useful in the present invention include compounds of the formula (V):



wherein R^1 , R^5 , R^6 , R^8 , and R^{11} are defined as above.

[0043] In other classes of compounds of formula **II-V**, R^1 is H or C_1 - C_6 alkyl. In certain compounds useful in the invention, R^1 is H, methyl, ethyl, *iso*-propyl, or *n*-propyl. In certain particular compounds, R^1 is methyl.

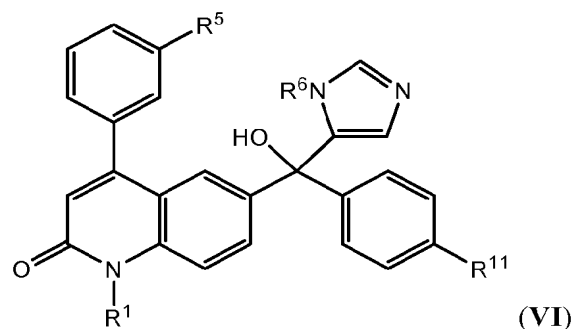
[0044] In yet other classes of compounds of formula **II-V**, R^5 is $-(CR^{13}R^{14})_tC\equiv CR^{16}$, wherein t is an integer from 0 to 5, inclusive, and R^{13} , R^{14} , and R^{16} are as defined above; and the other two R^3 and R^4 are H. In yet other compounds, R^5 is $-C\equiv CR^{16}$. For certain compounds, R^5 is C_2 - C_6 alkynyl. In other compounds, R^5 is $-C\equiv CH$.

[0045] In other classes of the compounds of formula **II-V**, R^6 is H. In other classes of the compounds of formula **II-V**, R^6 is C_1 - C_6 alkyl. In certain compounds, R^6 is methyl.

[0046] In yet other classes of the compounds of formula **II-V**, R^8 is H, $-OR^{12}$, or $-NR^{12}R^{13}$, wherein R^{12} and R^{13} are as defined above. R^8 is hydroxy or amino. In other compounds, R^8 is hydroxy. In yet other compounds, R^8 is amino.

[0047] In certain classes of the compounds of formula **II-V**, R^{11} is H, C_1 - C_{10} alkyl, halo, cyano, nitro, or amino. In certain compounds, R^{11} is halo, preferably chloro or fluoro. In certain particular compounds, R^{11} is chloro.

[0048] Compounds useful in the present invention include compounds of the formula (VI):



wherein R^1 , R^5 , R^6 , and R^{11} are defined as above.

[0049] In other classes of compounds of formula VI, R^1 is H or C_1 - C_6 alkyl. In certain compounds useful in the invention, R^1 is H, methyl, ethyl, *iso*-propyl, or *n*-propyl. In certain particular compounds, R^1 is methyl.

[0050] In yet other classes of compounds of formula VI, R^5 is $-(CR^{13}R^{14})_tC\equiv CR^{16}$, wherein t is an integer from 0 to 5, inclusive, and R^{13} , R^{14} , and R^{16} are as defined above; and the other two of R^3 , R^4 , and R^5 are H. For certain compounds, R^5 is C_2 - C_6 alkynyl. In other compounds, R^5 is $-C\equiv CH$.

[0051] In certain classes of the compounds of formula VI, R^{11} is H, C_1 - C_{10} alkyl, halo, cyano, nitro, or amino. In certain compounds, R^{11} is halo, preferably chloro or fluoro. In certain particular compounds, R^{11} is chloro.

[0052] Exemplary compounds useful in the present invention include the following:

6-[(4-Chloro-phenyl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-ethynyl-phenyl)-1-methyl-1H-quinolin-2-one (*R* enantiomer);

6-[(4-Chloro-phenyl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-ethynyl-phenyl)-1-methyl-1H-quinolin-2-one (*S* enantiomer);

6-[Amino-(4-chloro-phenyl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-ethynyl-phenyl)-1-methyl-1H-quinolin-2-one (*R* enantiomer);

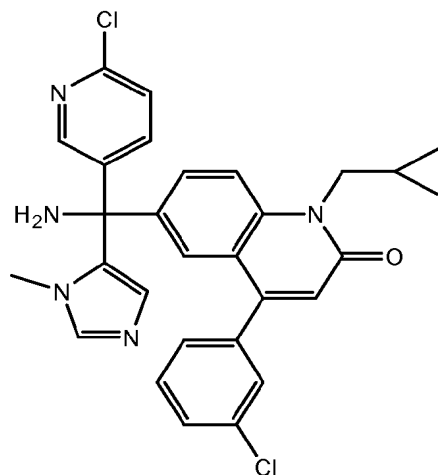
6-[Amino-(4-chloro-phenyl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-ethynyl-phenyl)-1-methyl-1H-quinolin-2-one (*S* enantiomer);

6-[(4-Chloro-phenyl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-ethynyl-4-fluoro-phenyl)-1-methyl-1H-quinolin-2-one;

6-[(4-chloro-phenyl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-4-[3-(3-hydroxy-3-methyl-but-1-ynyl)-phenyl]-1-methyl-1H-quinolin-2-one (*S* enantiomer); and

6-[(4-chloro-phenyl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-4-[3-(3-hydroxy-3-methyl-but-1-ynyl)-phenyl]-1-methyl-1H-quinolon-2-one (*R* enantiomer).

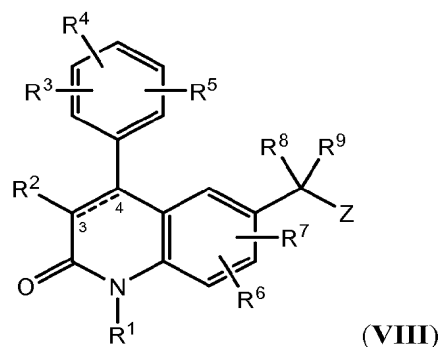
[0053] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (VII):



6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-cyclopropylmethyl-1H-quinoline-2-one (VII)

or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency. In certain embodiments, the tartrate salt of the compound is administered. In certain particular embodiments, the compound of formula VII useful in the invention is (+)-6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-cyclopropylmethyl-1H-quinoline-2-one. In certain particular embodiments, the compound of formula VII useful in the invention is (-)-6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-cyclopropylmethyl-1H-quinoline-2-one.

[0054] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject with a lysosomal storage disease a farnesyl transferase inhibitor of the formula (VIII):



wherein

the dashed line indicates an optional second bond connecting C-3 and C-4 of the quinolin-2-one ring;

R^1 selected from H, C_1-C_{10} alkyl, $-(CR^{13}R^{14})_qC(O)R^{12}$, $-(CR^{13}R^{14})_qC(O)OR^{15}$, $-(CR^{13}R^{14})_qC(O)R^{12}$, $-(CR^{13}R^{14})_qSO_2R^{15}$, $-(CR^{13}R^{14})_i(C_3-C_{10}$ cycloalkyl), $-(CR^{13}R^{14})_i(C_6-C_{10}$ aryl), and $-(CR^{13}R^{14})_i(4-10$ membered heterocyclic), wherein said cycloalkyl, aryl and heterocyclic R^1 groups are optionally fused to a C_6-C_{10} aryl group, a C_5-C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; and the foregoing R^1 groups, except H but including any optional fused rings referred to above, are optionally substituted by 1 to 4 R^6 groups;

R^2 is halo, cyano, $-C(O)OR^{15}$, or a group selected from the substituents provided in the definition of R^{12} ;

each R^3 , R^4 , R^5 , R^6 , and R^7 is independently selected from H, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-OR^{12}$, $-C(O)R^{12}$, $-C(O)OR^{12}$, $-NR^{13}C(O)OR^{15}$, $-OC(O)R^{12}$, $-NR^{13}SO_2R^{15}$, $-SO_2NR^{12}R^{13}$, $-NR^{13}C(O)R^{12}$, $-C(O)NR^{12}R^{13}$, $-NR^{12}R^{13}$, $-CH=NOR^{12}$, $-S(O)_jR^{12}$ wherein j is an integer from 0 to 2, $-(CR^{13}R^{14})_i(C_6-C_{10}$ aryl), $-(CR^{13}R^{14})_i(4-10$ membered heterocyclic), $-(CR^{13}R^{14})_i(C_3-C_{10}$ cycloalkyl), and $-(CR^{13}R^{14})_iC\equiv CR^{16}$; and wherein the cycloalkyl, aryl, and heterocyclic moieties of the foregoing groups are optionally fused to a C_6-C_{10} aryl group, a C_5-C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; and said alkyl, alkenyl, cycloalkyl, aryl and heterocyclic groups are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-NR^{13}SO_2R^{15}$, $-SO_2NR^{12}R^{13}$, $-C(O)R^{12}$, $-C(O)OR^{12}$, $-OC(O)R^{12}$, $-NR^{13}C(O)OR^{15}$, $-NR^{13}C(O)R^{12}$, $-C(O)NR^{12}R^{13}$, $-NR^{12}R^{13}$, $-OR^{12}$, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, $-(CR^{13}R^{14})_i(C_6-C_{10}$ aryl), and $-(CR^{13}R^{14})_i(4-10$ membered heterocyclic);

Z is an aromatic 4—10 membered heterocyclic group, substituted by 1 to 4 R⁶ substituents;

R⁸ is H, —OR¹², —OC(O)R¹², —NR¹²R¹³, —N=CR¹²R¹³, —NR¹²C(O)R¹³, cyano, —C(O)OR¹³, —SR¹², or —(CR¹³R¹⁴)_t(4—10 membered heterocyclic), wherein said heterocyclic R⁸ groups are substituted by 1 to 4 R⁶ groups;

R⁹ is —(CR¹³R¹⁴)_t(imidazolyl) or —(CR¹³R¹⁴)_t(pyridinyl) wherein said imidazolyl or pyridinyl moiety is substituted by 1 or 2 R⁶ substituents;

each R¹² is independently selected from H, C₁–C₁₀ alkyl, —(CR¹³R¹⁴)_t(C₃–C₁₀ cycloalkyl), —(CR¹³R¹⁴)_t(C₆–C₁₀ aryl), and —(CR¹³R¹⁴)_t(4—10 membered heterocyclic); said cycloalkyl, aryl and heterocyclic R¹² groups are optionally fused to a C₆–C₁₀ aryl group, a C₅–C₈ saturated cyclic group, or a 4—10 membered heterocyclic group; and the foregoing R¹² substituents, except H but including any optional fused rings, are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, —C(O)R¹³, —C(O)OR¹³, —OC(O)R¹³, —NR¹³C(O)R¹⁴, —C(O)NR¹³R¹⁴, —NR¹³R¹⁴, hydroxy, C₁–C₆ alkyl, and C₁–C₆ alkoxy;

each t is independently an integer from 0 to 5 and each q is independently an integer from 1 to 5;

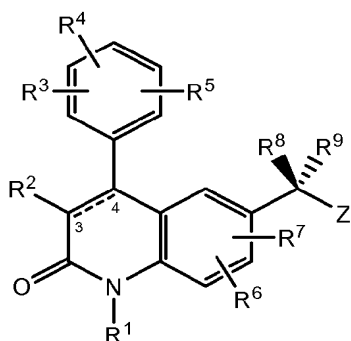
each R¹³ and R¹⁴ is independently H or C₁–C₆ alkyl, and where R¹³ and R¹⁴ are as —(CR¹³R¹⁴)_q or —(CR¹³R¹⁴)_t, each is independently defined for each iteration of q or t in excess of 1;

R¹⁵ is selected from the substituents provided in the definition of R¹² except R¹⁵ is not H;

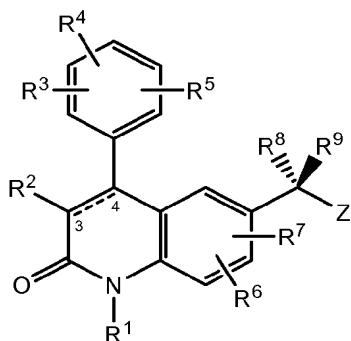
R¹⁶ is selected from the list of substituents provided in the definition of R¹² and —SiR¹⁷R¹⁸R¹⁹; and

R¹⁷, R¹⁸ and R¹⁹ are each independently selected from the substituents provided in the definition of R¹² except at least one of R¹⁷, R¹⁸ and R¹⁹ is not H; or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, salt, or other pharmaceutically acceptable form thereof, at a therapeutically effective dose and frequency. In certain embodiments, a racemate is used in the invention. In other embodiments, an enantiomerically pure compound is used. In other embodiments, an enantiomerically enriched mixture is used (*e.g.*, 70%, 75%, 80%, 90%, 95%, 98%, 99% of one enantiomer).

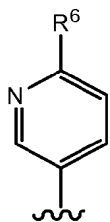
[0055] For certain compounds of formula VIII, the stereochemistry is defined as follows:



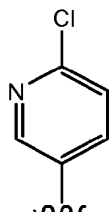
[0056] For other compounds of formula **VIII**, the stereochemistry is defined as follows:



[0057] In certain embodiments, compounds of formula **VIII** are those wherein Z is a 5 or 6 membered aromatic heterocyclic group substituted with from 1 to 4 R^6 substituents. In certain particular embodiments, compounds of formula **VIII** are those wherein Z is a pyridine or thiophene group substituted with from 1 to 4 R^6 substituents. In certain embodiments, Z is a pyridine group substituted with 1 to 4 R^6 substituents. In certain particular embodiments, Z is a pyridine group substituted with one R^6 substituent. In certain embodiments, Z is



. In certain particular embodiments, Z is a pyridine group substituted with one R^6 substituent, wherein the R^6 substituent is halo (*e.g.*, chloro). In certain particular



embodiments, Z is . In other embodiments, compounds of formula **VIII** are those

wherein Z is a 5 or 6 membered aromatic heterocyclic group fused to a benzene group, substituted with from 1 to 4 R^6 substituents. Preferably, Z comprises from 1 to 3 heteroatoms selected from O, S and N.

[0058] In certain embodiments, compounds of formula **VIII** are those wherein R^1 is H, C_1 – C_6 alkyl, or cyclopropylmethyl. In certain embodiments, R^1 is cyclopropylmethyl.

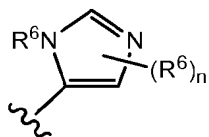
[0059] In certain embodiments, compounds of formula **VIII** are those wherein R^8 is — $NR^{12}R^{13}$, — OR^{12} , or — $(CR^{13}R^{14})$ (4–10 membered heterocyclic) substituted with from 1 to 4 R^6 groups, wherein said 4–10 membered heterocyclic is selected from triazolyl, imidazolyl, pyrazolyl, and piperidinyl. In certain embodiments, said heterocyclic is substituted with one R^6 group. In certain embodiments, R^8 is hydroxy, amino, or triazolyl. In certain embodiments, R^8 is hydroxy. In certain other embodiments, R^8 is amino.

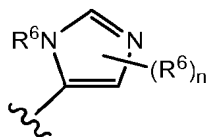
[0060] In certain embodiments, compounds of formula **VIII** are those wherein R^8 is H, — OR^{12} , — $OC(O)R^{12}$, — $NR^{12}R^{13}$, — $NR^{12}C(O)R^{13}$, cyano, — $C(O)OR^{13}$, — SR^{12} , or — $(CR^{13}R^{14})$ (4–10 membered heterocyclic), wherein said heterocyclic R^8 groups are substituted by 1 to 4 R^6 groups.

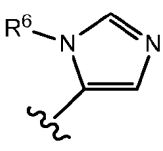
[0061] In certain embodiments, compounds of formula **VIII** are those wherein R^3 , R^4 , R^5 , and R^6 are independently selected from H, halo, and C_1 – C_6 alkoxy. In certain embodiments, one of R^3 , R^4 , and R^5 is halo (*e.g.*, chloro), and the others are hydrogen.

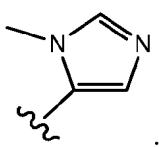
[0062] In certain embodiments, compounds of formula **VIII** are those wherein R^6 and R^7 are both hydrogen.

[0063] In certain embodiments, compound of formula **VIII** are those wherein R^9 is an imidazolyl moiety, optionally substituted with one or two R^6 substituents, wherein R^6 is defined as above. In certain compounds, R^9 is an imidazolyl moiety substituted with one R^6 substituents, wherein R^6 is defined as above. In certain compounds, R^9 is an imidazolyl moiety substituted with one R^6 substituents, wherein R^6 is C_1 – C_6 alkyl, preferably methyl. In

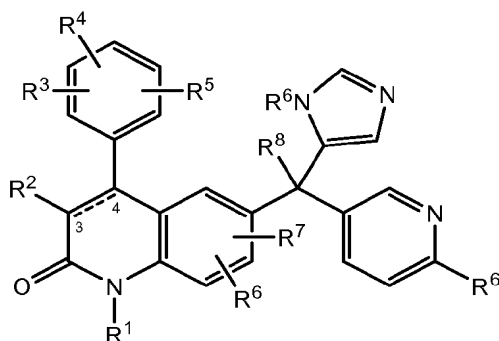


certain compounds, R^9 is , wherein R^6 is as defined above and t is an integer

between 0 and 2, inclusive. In other compounds, R^9 is , wherein R^6 is as defined

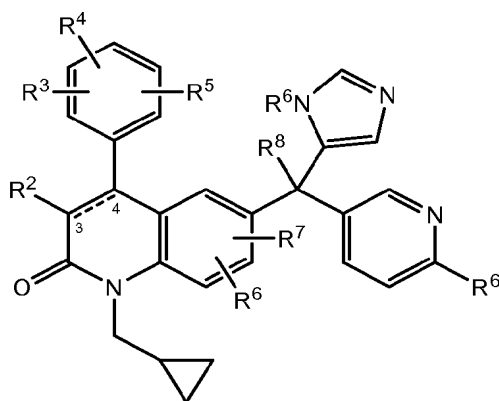
above. In other compounds, R^9 is .

[0064] Compounds useful in the present invention include compounds of the formula:



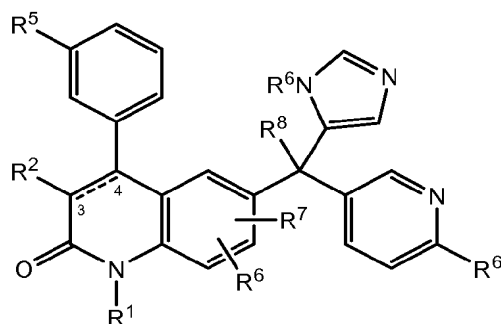
wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are defined as above.

[0065] Compounds useful in the present invention include compounds of the formula:



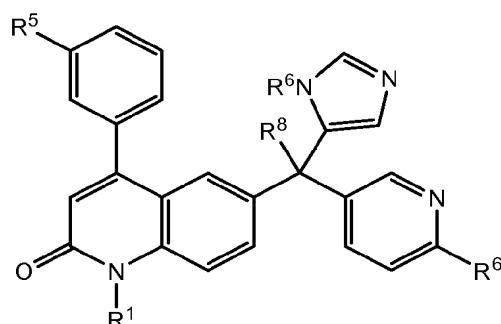
wherein R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are defined as above.

[0066] Compounds useful in the present invention include compounds of the formula:



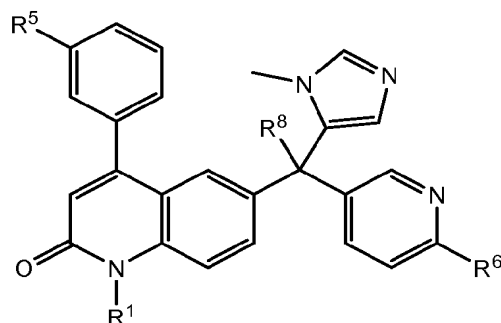
wherein R^1 , R^2 , R^5 , R^6 , R^7 , and R^8 are defined as above.

[0067] Compounds useful in the present invention include compounds of the formula:



wherein R^1 , R^5 , R^6 , and R^8 are defined as above.

[0068] Compounds useful in the present invention include compounds of the formula:



wherein R^1 , R^5 , R^6 , and R^8 are defined as above.

[0069] Exemplary compounds of the invention include:

6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-methyl-1H-quinolin-2-one (R enantiomer);

6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-methyl-1H-quinolin-2-one (S enantiomer);

4-(3-chloro-phenyl)-6-[(6-chloro-pyridin-3-yl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-1-cyclopropylmethyl-1H-quinolin-2-one;

6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-cyclopropylmethyl-1H-quinolin-2-one;

4-(3-chloro-phenyl)-6-[(5-chloro-pyridin-2-yl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-1-methyl-1H-quinolin-2-one;

6-[amino-(5-chloro-pyridin-2-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-methyl-1H-quinolin-2-one;

6-[amino-(5-chloro-pyridin-2-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-cyclopropylmethyl-1H-quinolin-2-one;

6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3,5-dichloro-phenyl)-1-methyl-1H-quinolin-2-one;

6-[amino-(5-chloro-thiophen-2-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-methyl-1H-quinolin-2-one;

6-[(5-chloro-thiophen-2-yl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-ethoxy-phenyl)-1-methyl-1H-quinolin-2-one;

amino-(5-chloro-thiophen-2-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-ethoxy-phenyl)-1-methyl-1H-quinolin-2-one;

6-[(6-chloro-pyridin-3-yl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-ethoxy-phenyl)-1-methyl-1H-quinolin-2-one;

6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-ethoxy-phenyl)-1-methyl-1H-quinolin-2-one;

6[benzo[b]thiophen-2-yl-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-methyl-1H-quinolin-2-one;

6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1H-quinolin-2-one;

(-)-6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-cyclopropylmethyl-1H-quinolin-2-one;

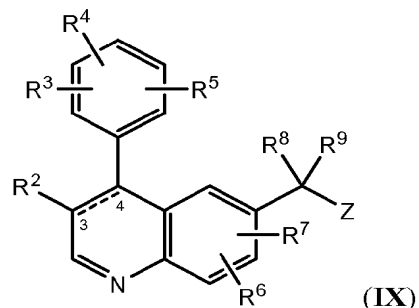
6-[amino-(6-methyl-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-methyl-1H-quinolin-2-one;

6-[amino-(6-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-cyclopropylmethyl-1H-quinolin-2-one;

(+)-4-(3-chloro-phenyl)-6-[(6-chloro-pyridin-3-yl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-1-cyclopropylmethyl-1H-quinolin-2-one; and

pharmaceutically acceptable derivatives, analogs, stereoisomers, isomers, solvates, salts, or other pharmaceutically acceptable forms of the foregoing compounds.

[0070] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (IX):



wherein

the dashed line indicates an optional second bond connecting C-3 and C-4 of the quinoline ring;

R^2 is halo, cyano, $-\text{C}(\text{O})\text{OR}^{15}$, or a group selected from the substituents provided in the definition of R^{12} ;

each R^3 , R^4 , R^5 , R^6 , and R^7 is independently selected from H, $\text{C}_1\text{--C}_{10}$ alkyl, $\text{C}_2\text{--C}_{10}$ alkenyl, $\text{C}_2\text{--C}_{10}$ alkynyl, halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-\text{OR}^{12}$, $-\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{OR}^{12}$, $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{15}$, $-\text{OC}(\text{O})\text{R}^{12}$, $-\text{NR}^{13}\text{SO}_2\text{R}^{15}$, $-\text{SO}_2\text{NR}^{12}\text{R}^{13}$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{NR}^{12}\text{R}^{13}$, $-\text{NR}^{12}\text{R}^{13}-\text{CH}=\text{NOR}^{12}-\text{S}(\text{O})\text{R}^{12}$ wherein j is an integer from 0 to 2, $-(\text{CR}^{13}\text{R}^{14})_i(\text{C}_6\text{--C}_{10}\text{ aryl})$, $-(\text{CR}^{13}\text{R}^{14})_i(4\text{--}10\text{ membered heterocyclic})$, $-(\text{CR}^{13}\text{R}^{14})$, $-(\text{C}_3\text{--C}_{10}\text{ cycloalkyl})$, and $-(\text{CR}^{13}\text{R}^{14})_i\text{C}\equiv\text{CR}^{16}$; and wherein the cycloalkyl, aryl, and heterocyclic moieties of the foregoing groups are optionally fused to a $\text{C}_6\text{--C}_{10}$ aryl group, a $\text{C}_5\text{--C}_8$ saturated cyclic group, or a 4-10 membered heterocyclic group; and said alkyl, alkenyl, cycloalkyl, aryl and heterocyclic groups are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-\text{NR}^{13}\text{SO}_2\text{R}^{15}$, $-\text{SO}_2\text{NR}^{12}\text{R}^{13}$, $-\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{OR}^{12}$, $-\text{OC}(\text{O})\text{R}^{12}$, $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{15}$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{NR}^{12}\text{R}^{13}$, $-\text{NR}^{12}\text{R}^{13}$, $-\text{OR}^{12}$, $\text{C}_1\text{--C}_{10}$ alkyl, $\text{C}_2\text{--C}_{10}$ alkenyl, $\text{C}_2\text{--C}_{10}$ alkynyl, $-(\text{CR}^{13}\text{R}^{14})_i(\text{C}_6\text{--C}_{10}\text{ aryl})$, and $-(\text{CR}^{13}\text{R}^{14})_i(4\text{--}10\text{ membered heterocyclic})$;

Z is an aromatic 4-10 membered heterocyclic group, substituted by 1 to 4 R^6 substituents;

R^8 is H, $-\text{OR}^{12}$, $-\text{OC}(\text{O})\text{R}^{12}$, $-\text{NR}^{12}\text{R}^{13}$, $-\text{NR}^{12}\text{C}(\text{O})\text{R}^{13}$, cyano, $-\text{C}(\text{O})\text{OR}^{13}$, $-\text{SR}^{12}$, or $-(\text{CR}^{13}\text{R}^{14})_i(4\text{--}10\text{ membered heterocyclic})$, wherein said heterocyclic R^8 groups are substituted by 1 to 4 R^6 groups;

R^9 is $-(CR^{13}R^{14})_t$ (imidazolyl) or $-(CR^{13}R^{14})_t$ (pyridinyl), wherein said imidazolyl or pyridinyl moiety is substituted by 1 or 2 R^6 substituents;

each R^{12} is independently selected from H, C_1 - C_{10} alkyl, $-(CR^{13}R^{14})_t$ (C_3 - C_{10} cycloalkyl), $-(CR^{13}R^{14})_t$ (C_6 - C_{10} aryl), and $-(CR^{13}R^{14})_t$ (4-10 membered heterocyclic); said cycloalkyl, aryl, and heterocyclic R^{12} groups are optionally fused to a C_6 - C_{10} aryl group, a C_5 - C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; and the foregoing R^{12} substituents, except H but including any optional fused rings, are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NR^{13}C(O)R^{14}$, $-C(O)NR^{13}R^{14}$, $-NR^{13}R^{14}$, hydroxy, C_1 - C_6 alkyl, and C_1 - C_6 alkoxy;

each t is independently an integer from 0 to 5;

each R^{13} and R^{14} is independently H or C_1 - C_6 alkyl, and where R^{13} and R^{14} are as $-(CR^{13}R^{14})_t$, each is independently defined for each iteration of t in excess of 1;

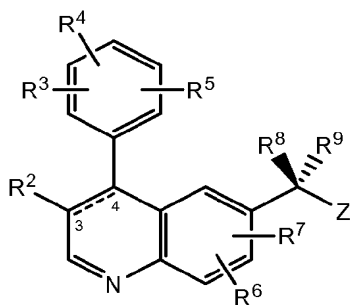
R^{15} is selected from the substituents provided in the definition of R^{12} except R^{15} is not H;

R^{16} is selected from the list of substituents provided in the definition of R^{12} and $-SiR^{17}R^{18}R^{19}$; and,

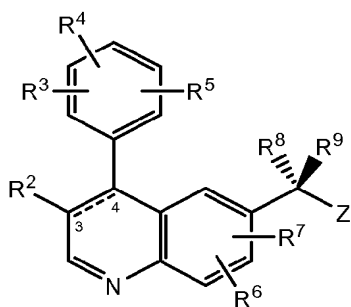
R^{17} , R^{18} and R^{19} are each independently selected from the substituents provided in the definition of R^{12} except at least one of R^{17} , R^{18} and R^{19} is not H;

or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, salt, or other pharmaceutically acceptable forms thereof, at a therapeutically effective dose and frequency. In certain embodiments, a racemate is used in the invention. In other embodiments, an enantiomerically pure compound is used. In other embodiments, an enantiomerically enriched mixture is used (*e.g.*, 70%, 75%, 80%, 90%, 95%, 98%, 99% of one enantiomer).

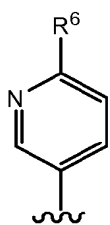
[0071] For certain compounds of formula IX, the stereochemistry is defined as follows:



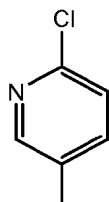
[0072] For other compounds of formula IX, the stereochemistry is defined as follows:



[0073] In certain embodiments, compounds of formula **IX** are those wherein Z is a 5 or 6 membered aromatic heterocyclic group substituted with from 1 to 4 R^6 substituents. In certain particular embodiments, compounds of formula **IX** are those wherein Z is a pyridine or thiophene group substituted with from 1 to 4 R^6 substituents. In certain embodiments, Z is a pyridine group substituted with 1 to 4 R^6 substituents. In certain particular embodiments, Z is a pyridine group substituted with one R^6 substituent. In certain embodiments, Z is



. In certain particular embodiments, Z is a pyridine group substituted with one R^6 substituent, wherein the R^6 substituent is halo (*e.g.*, chloro). In certain particular



embodiments, Z is . In other embodiments, compounds of formula **IX** are those wherein Z is a 5 or 6 membered aromatic heterocyclic group fused to a benzene group, substituted with from 1 to 4 R^6 substituents. Preferably, Z comprises from 1 to 3 heteroatoms selected from O, S and N.

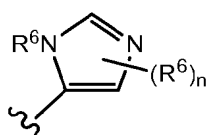
[0074] In certain embodiments, compounds of formula **IX** are those wherein R^8 is — $NR^{12}R^{13}$, — OR^{12} , or — $(CR^{13}R^{14})_n$ (4–10 membered heterocyclic) substituted with from 1 to 4 R^6 groups, wherein said 4–10 membered heterocyclic is selected from triazolyl, imidazolyl, pyrazolyl, and piperidiny. In certain embodiments, said heterocyclic is substituted with one R^6 group. In certain embodiments, R^8 is hydroxy, amino, or triazolyl. In certain embodiments, R^8 is hydroxy. In certain other embodiments, R^8 is amino.

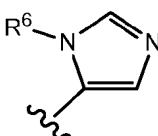
[0075] In certain embodiments, compounds of formula **IX** are those wherein R^8 is H, —OR¹², —OC(O)R¹², —NR¹²R¹³, —NR¹²C(O)R¹³, cyano, —C(O)OR¹³, —SR¹², or —(CR¹³R¹⁴)_n (4–10 membered heterocyclic), wherein said heterocyclic R⁸ groups are substituted by 1 to 4 R⁶ groups.

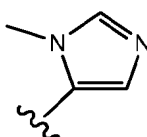
[0076] In certain embodiments, compounds of formula **IX** are those wherein R³, R⁴, R⁵, and R⁶ are independently selected from H, halo, and C₁–C₆ alkoxy. In certain embodiments, one of R³, R⁴, and R⁵ is halo (*e.g.*, chloro), and the others are hydrogen.

[0077] In certain embodiments, compounds of formula **IX** are those wherein R⁶ and R⁷ are both hydrogen.

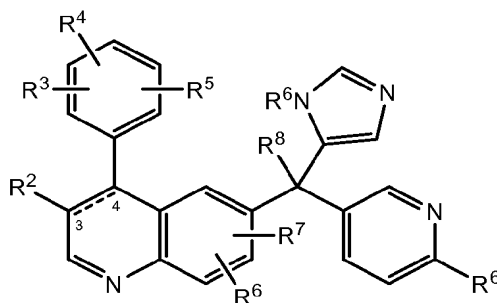
[0078] In certain embodiments, compound of formula **IX** are those wherein R⁹ is an imidazolyl moiety, optionally substituted with one or two R⁶ substituents, wherein R⁶ is defined as above. In certain compounds, R⁹ is an imidazolyl moiety substituted with one R⁶ substituents, wherein R⁶ is defined as above. In certain compounds, R⁹ is an imidazolyl moiety substituted with one R⁶ substituents, wherein R⁶ is C₁–C₆ alkyl, preferably methyl. In

certain compounds, R⁹ is , wherein R⁶ is as defined above and t is an integer

between 0 and 2, inclusive. In other compounds, R⁹ is , wherein R⁶ is as defined

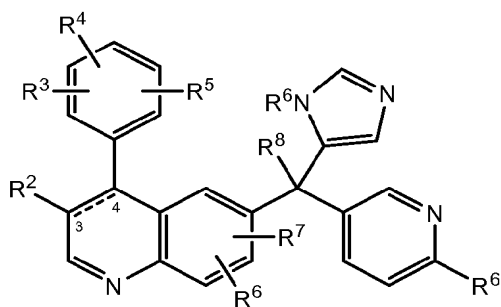
above. In other compounds, R⁹ is .

[0079] Compounds useful in the present invention include compounds of the formula:



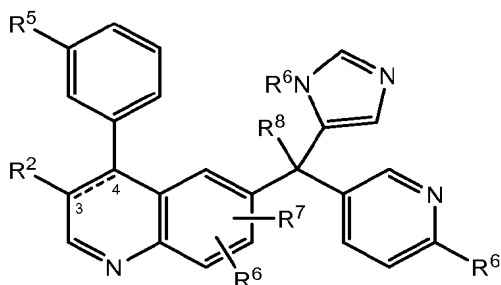
wherein R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ are defined as above.

[0080] Compounds useful in the present invention include compounds of the formula:



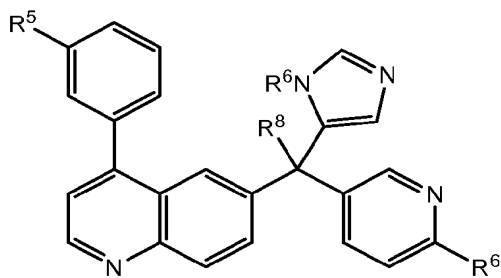
wherein R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are defined as above.

[0081] Compounds useful in the present invention include compounds of the formula:



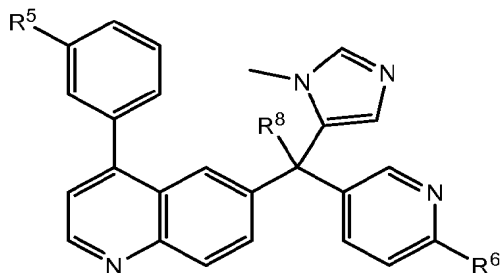
wherein R^2 , R^5 , R^6 , R^7 , and R^8 are defined as above.

[0082] Compounds useful in the present invention include compounds of the formula:



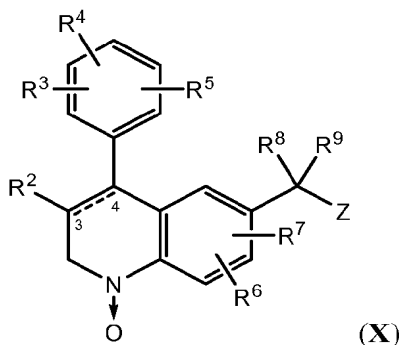
wherein R^5 , R^6 , and R^8 are defined as above.

[0083] Compounds useful in the present invention include compounds of the formula:



wherein R^5 , R^6 , and R^8 are defined as above.

[0084] In another embodiment, the invention is a method for treating a subject comprising administering to the subject with a lysosomal storage disease a farnesyl transferase inhibitor of the formula (X):



wherein

the dashed line indicates an optional second bond connecting C-3 and C-4 of the quinoline ring;

R^2 is halo, cyano, $-\text{C}(\text{O})\text{OR}^{15}$, or a group selected from the substituents provided in the definition of R^{12} ;

each R^3 , R^4 , R^5 , R^6 , and R^7 is independently selected from H, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-\text{OR}^{12}$, $-\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{OR}^{12}$, $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{15}$, $-\text{OC}(\text{O})\text{R}^{12}$, $-\text{NR}^{13}\text{SO}_2\text{R}^{15}$, $-\text{SO}_2\text{NR}^{12}\text{R}^{13}$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{NR}^{12}\text{R}^{13}$, $-\text{NR}^{12}\text{R}^{13}$, $-\text{CH}=\text{NOR}^{12}$, $-\text{S}(\text{O})_j\text{R}^{12}$ wherein j is an integer from 0 to 2, $-(\text{CR}^{13}\text{R}^{14})_i(\text{C}_6\text{-C}_{10}\text{ aryl})$, $-(\text{CR}^{13}\text{R}^{14})_i(4\text{-}10\text{ membered heterocyclic})$, $-(\text{CR}^{13}\text{R}^{14})_i(\text{C}_3\text{-C}_{10}\text{ cycloalkyl})$, and $-(\text{CR}^{13}\text{R}^{14})_i\text{C}\equiv\text{CR}^{16}$; and wherein the cycloalkyl, aryl and heterocyclic moieties of the foregoing groups are optionally fused to a $\text{C}_6\text{-C}_{10}$ aryl group, a $\text{C}_1\text{-C}_8$ saturated cyclic group, or a 4-10 membered heterocyclic group; and said alkyl, alkenyl, cycloalkyl, aryl and heterocyclic groups are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-\text{NR}^{13}\text{SO}_2\text{R}^{15}$, $-\text{SO}_2\text{NR}^{12}\text{R}^{13}$, $-\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{OR}^{12}$, $-\text{OC}(\text{O})\text{R}^{12}$, $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{15}$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{NR}^{12}\text{R}^{13}$, $-\text{NR}^{12}\text{R}^{13}$, $-\text{OR}^{12}$, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, $-(\text{CR}^{13}\text{R}^{14})_i(\text{C}_6\text{-C}_{10}\text{ aryl})$, and $-(\text{CR}^{13}\text{R}^{14})_i(4\text{-}10\text{ membered heterocyclic})$;

Z is an aromatic 4-10 membered heterocyclic group, substituted by 1 to 4 R^6 substituents;

R^8 is H, $—OR^{12}$, $—OC(O)R^{12}$, $—NR^{12}R^{13}$, $—NR^{12}C(O)R^{13}$, cyano, $—C(O)OR^{13}$, $—SR^{12}$, or $—(CR^{13}R^{14})_t$ (4-10 membered heterocyclic), wherein said heterocyclic R^8 groups are substituted by 1 to 4 R^6 groups;

R^9 is $—(CR^{13}R^{14})_t$ (imidazolyl) or $—(CR^{13}R^{14})_t$ (pyridinyl) wherein said imidazolyl or pyridinyl moiety is substituted by 1 or 2 R^6 substituents;

each R^{12} is independently selected from H, C_1 - C_{10} alkyl, $—(CR^{13}R^{14})_t$ (C_3 - C_{10} cycloalkyl), $—(CR^{13}R^{14})_t$ (C_6 - C_{10} aryl), and $—(CR^{13}R^{14})_t$ (4-10 membered heterocyclic); said cycloalkyl, aryl, and heterocyclic R^{12} groups are optionally fused to a C_6 - C_{10} aryl group, a C_5 - C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; and the foregoing R^{12} substituents, except H but including any optional fused rings, are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $—C(O)R^{13}$, $—C(O)OR^{13}$, $—OC(O)R^{13}$, $—NR^{13}C(O)R^{14}$, $—C(O)NR^{13}R^{14}$, $—NR^{13}R^{14}$, hydroxy, C_1 - C_6 alkyl, and C_1 - C_6 alkoxy;

each t is independently an integer from 0 to 5;

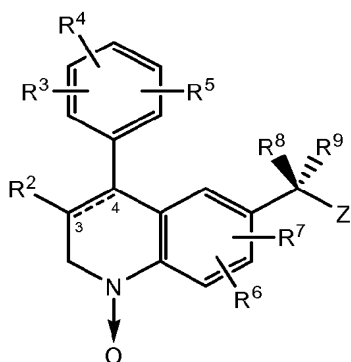
each R^{13} and R^{14} is independently H or C_1 - C_6 alkyl, and where R^{13} and R^{14} are as $—(CR^{13}R^{14})_t$, each is independently defined for each iteration of t in excess of 1; R^{15} is selected from the substituents provided in the definition of R^{12} except R^{15} is not H;

R^{16} is selected from the list of substituents provided in the definition of R^{12} and $—SiR^{17}R^{18}R^{19}$; and,

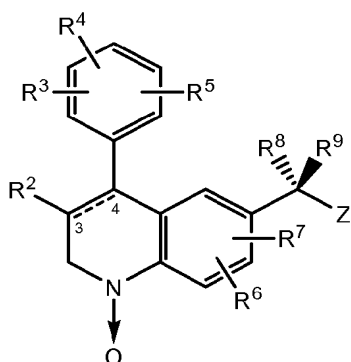
R^{17} , R^{18} and R^{19} are each independently selected from the substituents provided in the definition of R^{12} , except at least one of R^{17} , R^{18} , and R^{19} is not H;

or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, salt, or other pharmaceutically acceptable form thereof, at a therapeutically effective dose and frequency. In certain embodiments, a racemate is used in the invention. In other embodiments, an enantiomerically pure compound is used. In other embodiments, an enantiomerically enriched mixture is used (*e.g.*, 70%, 75%, 80%, 90%, 95%, 98%, 99% of one enantiomer).

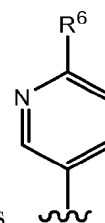
[0085] For certain compounds of formula **X**, the stereochemistry is defined as follows:




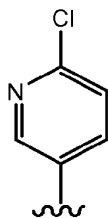
[0086] For other compounds of formula **X**, the stereochemistry is defined as follows:




[0087] In certain embodiments, compounds of formula **X** are those wherein Z is a 5 or 6 membered aromatic heterocyclic group substituted with from 1 to 4 R^6 substituents. In certain particular embodiments, compounds of formula **X** are those wherein Z is a pyridine or thiophene group substituted with from 1 to 4 R^6 substituents. In certain embodiments, Z is a pyridine group substituted with 1 to 4 R^6 substituents. In certain particular embodiments, Z is



a pyridine group substituted with one R^6 substituent. In certain embodiments, Z is . In certain particular embodiments, Z is a pyridine group substituted with one R^6 substituent, wherein the R^6 substituent is halo (*e.g.*, chloro). In certain particular embodiments, Z is



. In other embodiments, compounds of formula **X** are those wherein Z is a 5 or 6

membered aromatic heterocyclic group fused to a benzene group, substituted with from 1 to 4 R^6 substituents. Preferably, Z comprises from 1 to 3 heteroatoms selected from O, S and N.

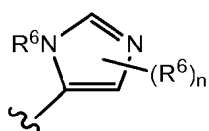
[0088] In certain embodiments, compounds of formula **X** are those wherein R^8 is — $NR^{12}R^{13}$, — OR^{12} , or — $(CR^{13}R^{14})$ (4–10 membered heterocyclic) substituted with from 1 to 4 R^6 groups, wherein said 4–10 membered heterocyclic is selected from triazolyl, imidazolyl, pyrazolyl, and piperidiny. In certain embodiments, said heterocyclic is substituted with one R^6 group. In certain embodiments, R^8 is hydroxy, amino, or triazolyl. In certain embodiments, R^8 is hydroxy. In certain other embodiments, R^8 is amino.

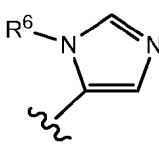
[0089] In certain embodiments, compounds of formula **X** are those wherein R^8 is H, — OR^{12} , — $OC(O)R^{12}$, — $NR^{12}R^{13}$, — $NR^{12}C(O)R^{13}$, cyano, — $C(O)OR^{13}$, — SR^{12} , or — $(CR^{13}R^{14})$ (4–10 membered heterocyclic), wherein said heterocyclic R^8 groups are substituted by 1 to 4 R^6 groups.

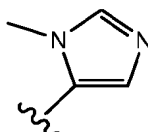
[0090] In certain embodiments, compounds of formula **X** are those wherein R^3 , R^4 , R^5 , and R^6 are independently selected from H, halo, and C_1 – C_6 alkoxy. In certain embodiments, one of R^3 , R^4 , and R^5 is halo (*e.g.*, chloro), and the others are hydrogen.

[0091] In certain embodiments, compounds of formula **X** are those wherein R^6 and R^7 are both hydrogen.

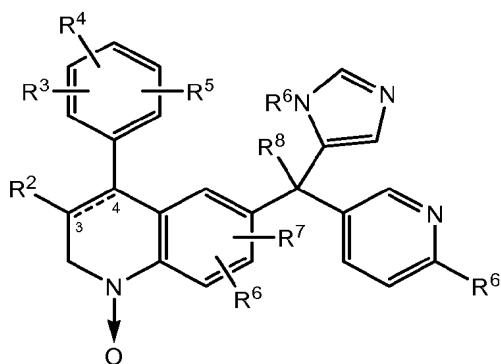
[0092] In certain embodiments, compound of formula **X** are those wherein R^9 is an imidazolyl moiety, optionally substituted with one or two R^6 substituents, wherein R^6 is defined as above. In certain compounds, R^9 is an imidazolyl moiety substituted with one R^6 substituents, wherein R^6 is defined as above. In certain compounds, R^9 is an imidazolyl moiety substituted with one R^6 substituents, wherein R^6 is C_1 – C_6 alkyl, preferably methyl. In

certain compounds, R^9 is , wherein R^6 is as defined above and t is an integer

between 0 and 2, inclusive. In other compounds, R^9 is , wherein R^6 is as defined

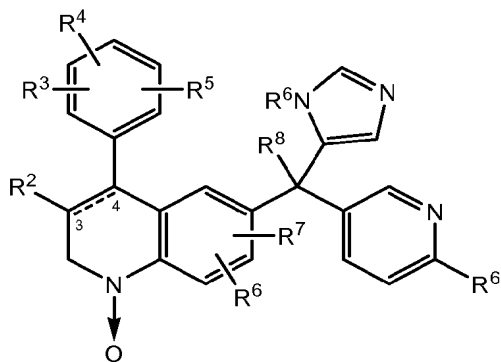
above. In other compounds, R^9 is .

[0093] Compounds useful in the present invention include compounds of the formula:



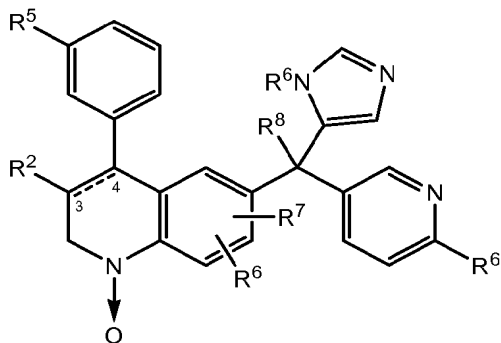
wherein R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are defined as above.

[0094] Compounds useful in the present invention include compounds of the formula:



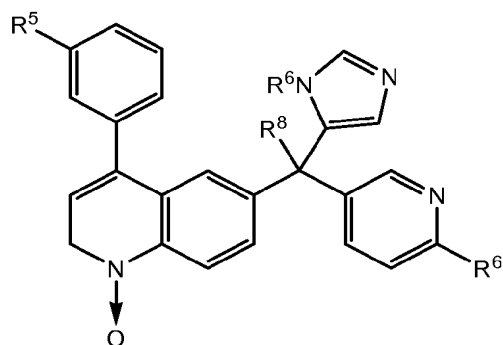
wherein R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are defined as above.

[0095] Compounds useful in the present invention include compounds of the formula:



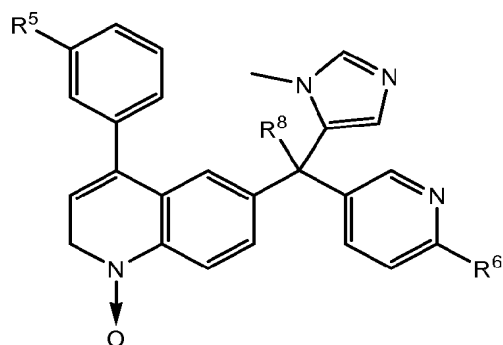
wherein R^2 , R^5 , R^6 , R^7 , and R^8 are defined as above.

[0096] Compounds useful in the present invention include compounds of the formula:



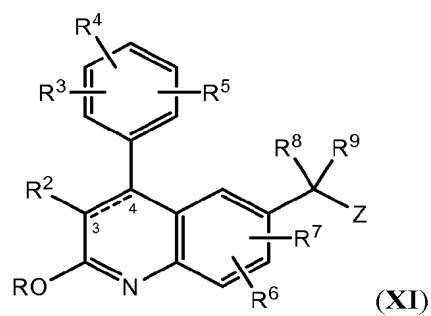
wherein R^5 , R^6 , and R^8 are defined as above.

[0097] Compounds useful in the present invention include compounds of the formula:



wherein R^5 , R^6 , and R^8 are defined as above.

[0098] In another embodiment, the invention is a method for treating a subject comprising administering to the subject with a lysosomal storage disease a farnesyl transferase inhibitor of the formula (XI):



wherein

the dashed line indicates an optional second bond connecting C-3 and C-4 of the quinoline ring;

R is C_1-C_6 alkyl;

R^2 is halo, cyano, $-\text{C}(\text{O})\text{OR}^{15}$, or a group selected from the substituents provided in the definition of R^{12} ;

each R^3 , R^4 , R^5 , R^6 , and R^7 is independently selected from H, $\text{C}_1\text{--C}_{10}$ alkyl, $\text{C}_2\text{--C}_{10}$ alkenyl, $\text{C}_2\text{--C}_{10}$ alkynyl, halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-\text{OR}^{12}$, $-\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{OR}^{12}$, $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{15}$, $-\text{OC}(\text{O})\text{R}^{12}$, $-\text{NR}^{13}\text{SO}_2\text{R}^{15}$, $-\text{SO}_2\text{NR}^{12}\text{R}^{13}$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{NR}^{12}\text{R}^{13}$, $-\text{NR}^{12}\text{R}^{13}$, $-\text{CH}=\text{NOR}^{12}$, $-\text{S}(\text{O})_j\text{R}^{12}$ wherein j is an integer from 0 to 2, $-(\text{CR}^{13}\text{R}^{14})_i(\text{C}_6\text{--C}_{10} \text{ aryl})$, $-(\text{CR}^{13}\text{R}^{14})_i(4\text{--}10 \text{ membered heterocyclic})$, $-(\text{CR}^{13}\text{R}^{14})_i(\text{C}_3\text{--C}_{10} \text{ cycloalkyl})$, and $-(\text{CR}^{13}\text{R}^{14})_i\text{C}\equiv\text{CR}^{16}$; and wherein the cycloalkyl, aryl, and heterocyclic moieties of the foregoing groups are optionally fused to a $\text{C}_6\text{--C}_{10}$ aryl group, a $\text{C}_5\text{--C}_8$ saturated cyclic group, or a 4–10 membered heterocyclic group; and said alkyl, alkenyl, cycloalkyl, aryl, and heterocyclic groups are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-\text{NR}^{13}\text{SO}_2\text{R}^{15}$, $-\text{SO}_2\text{NR}^{12}\text{R}^{13}$, $-\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{OR}^{12}$, $-\text{OC}(\text{O})\text{R}^{12}$, $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{15}$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{NR}^{12}\text{R}^{13}$, $-\text{NR}^{12}\text{R}^{13}$, $-\text{OR}^{12}$, $\text{C}_1\text{--C}_{10}$ alkyl, $\text{C}_2\text{--C}_{10}$ alkenyl, $\text{C}_2\text{--C}_{10}$ alkynyl, $-(\text{CR}^{13}\text{R}^{14})_i(\text{C}_6\text{--C}_{10} \text{ aryl})$, and $-(\text{CR}^{13}\text{R}^{14})_i(4\text{--}10 \text{ membered heterocyclic})$;

Z is an aromatic 4–10 membered heterocyclic group, substituted by 1 to 4 R^6 substituents;

R^8 is H, $-\text{OR}^{12}$, $-\text{OC}(\text{O})\text{R}^{12}$, $-\text{NR}^{12}\text{R}^{13}$, $-\text{R}^{12}\text{C}(\text{O})\text{R}^{13}$, cyano, $-(\text{O})\text{OR}^{13}$, $-\text{R}^{12}$, or $-(\text{CR}^{12}\text{R}^{14})_i(4\text{--}10 \text{ membered heterocyclic})$, wherein said heterocyclic R^8 groups are substituted by 1 to 4 R^6 groups;

R^9 is $-(\text{CR}^{13}\text{R}^{14})_i(\text{imidazolyl})$ or $-(\text{CR}^{13}\text{R}^{14})_i(\text{pyridinyl})$, wherein said imidazolyl or pyridinyl moiety is substituted by 1 or 2 R^6 substituents;

each R^{12} is independently selected from H, $\text{C}_1\text{--C}_{10}$ alkyl, $-(\text{CR}^{13}\text{R}^{14})_i(\text{C}_3\text{--C}_{10} \text{ cycloalkyl})$, $-(\text{CR}^{13}\text{R}^{14})_i(\text{C}_6\text{--C}_{10} \text{ aryl})$, and $-(\text{CR}^{13}\text{R}^{14})_i(4\text{--}10 \text{ membered heterocyclic})$; said cycloalkyl, aryl, and heterocyclic R^{12} groups are optionally fused to a $\text{C}_6\text{--C}_{10}$ aryl group, a $\text{C}_5\text{--C}_8$ saturated cyclic group, or a 4–10 membered heterocyclic group; and the foregoing R^{12} substituents, except H but including any optional fused rings, are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-\text{C}(\text{O})\text{R}^{13}$, $-\text{C}(\text{O})\text{OR}^{13}$, $-\text{OC}(\text{O})\text{R}^{13}$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{14}$, $-\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$, $-\text{NR}^{13}\text{R}^{14}$, hydroxy, $\text{C}_1\text{--C}_6$ alkyl, and $\text{C}_1\text{--C}_6$ alkoxy;

each t is independently an integer from 0 to 5;

each R^{13} and R^{14} is independently H or $\text{C}_1\text{--C}_6$ alkyl, and where R^{13} and R^{14} are as $-(\text{CR}^{13}\text{R}^{14})_i$, each is independently defined for each iteration of t in excess of 1;

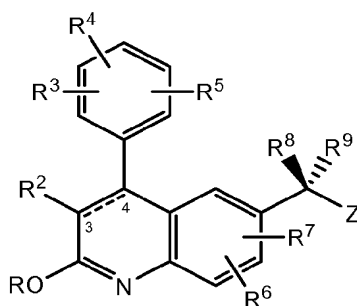
R^{15} is selected from the substituents provided in the definition of R^{12} except R^{15} is not H;

R^{16} is selected from the list of substituents provided in the definition of R^{12} and —
SiR¹⁷R¹⁸R¹⁹; and,

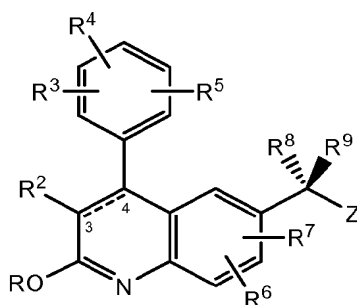
R^{17} , R^{18} and R^{19} are each independently selected from the substituents provided in the definition of R^{12} except at least one of R^{17} , R^{18} and R^{19} is not H;

or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, salt, or other pharmaceutically acceptable form thereof, at a therapeutically effective dose and frequency. In certain embodiments, a racemate is used in the invention. In other embodiments, an enantiomerically pure compound is used. In other embodiments, an enantiomerically enriched mixture is used (e.g., 70%, 75%, 80%, 90%, 95%, 98%, 99% of one enantiomer).

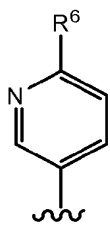
[0099] For certain compounds of formula **XI**, the stereochemistry is defined as follows:



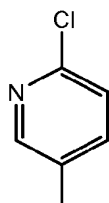
[00100] For other compounds of formula **XI**, the stereochemistry is defined as follows:



[00101] In certain embodiments, compounds of formula **XI** are those wherein Z is a 5 or 6 membered aromatic heterocyclic group substituted with from 1 to 4 R^6 substituents. In certain particular embodiments, compounds of formula **XI** are those wherein Z is a pyridine or thiophene group substituted with from 1 to 4 R^6 substituents. In certain embodiments, Z is a pyridine group substituted with 1 to 4 R^6 substituents. In certain particular embodiments, Z is a pyridine group substituted with one R^6 substituent. In certain embodiments, Z is



. In certain particular embodiments, Z is a pyridine group substituted with one R^6 substituent, wherein the R^6 substituent is halo (*e.g.*, chloro). In certain particular



embodiments, Z is . In other embodiments, compounds of formula **XI** are those wherein Z is a 5 or 6 membered aromatic heterocyclic group fused to a benzene group, substituted with from 1 to 4 R^6 substituents. Preferably, Z comprises from 1 to 3 heteroatoms selected from O, S and N.

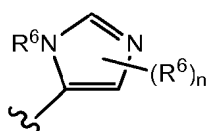
[00102] In certain embodiments, compounds of formula **XI** are those wherein R^8 is — $NR^{12}R^{13}$, — OR^{12} , or — $(CR^{13}R^{14})_n$ (4–10 membered heterocyclic) substituted with from 1 to 4 R^6 groups, wherein said 4–10 membered heterocyclic is selected from triazolyl, imidazolyl, pyrazolyl, and piperidiny. In certain embodiments, said heterocyclic is substituted with one R^6 group. In certain embodiments, R^8 is hydroxy, amino, or triazolyl. In certain embodiments, R^8 is hydroxy. In certain other embodiments, R^8 is amino.

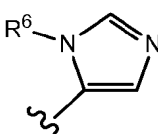
[00103] In certain embodiments, compounds of formula **XI** are those wherein R^8 is H, — OR^{12} , — $OC(O)R^{12}$, — $NR^{12}R^{13}$, — $NR^{12}C(O)R^{13}$, cyano, — $C(O)OR^{13}$, — SR^{12} , or — $(CR^{13}R^{14})_n$ (4–10 membered heterocyclic), wherein said heterocyclic R^8 groups are substituted by 1 to 4 R^6 groups.

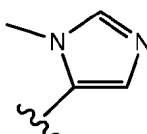
[00104] In certain embodiments, compounds of formula **XI** are those wherein R^3 , R^4 , R^5 , and R^6 are independently selected from H, halo, and C_1 – C_6 alkoxy. In certain embodiments, one of R^3 , R^4 , and R^5 is halo (*e.g.*, chloro), and the others are hydrogen.

[00105] In certain embodiments, compounds of formula **XI** are those wherein R^6 and R^7 are both hydrogen.

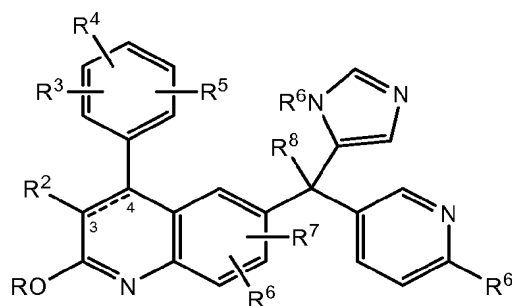
[00106] In certain embodiments, compound of formula **XI** are those wherein R^9 is an imidazolyl moiety, optionally substituted with one or two R^6 substituents, wherein R^6 is defined as above. In certain compounds, R^9 is an imidazolyl moiety substituted with one R^6 substituents, wherein R^6 is defined as above. In certain compounds, R^9 is an imidazolyl moiety substituted with one R^6 substituents, wherein R^6 is C_1 – C_6 alkyl, preferably methyl. In

certain compounds, R^9 is , wherein R^6 is as defined above and t is an integer

between 0 and 2, inclusive. In other compounds, R^9 is , wherein R^6 is as defined

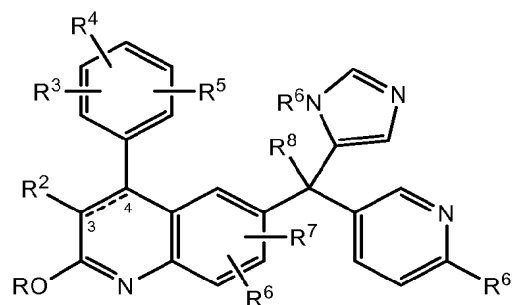
above. In other compounds, R^9 is .

[00107] Compounds useful in the present invention include compounds of the formula:



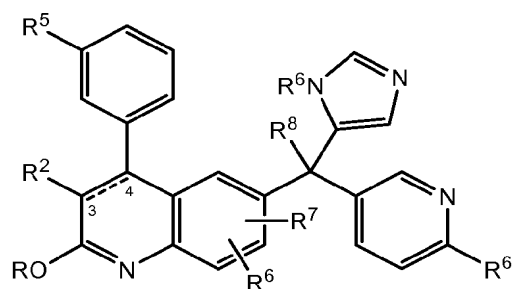
wherein R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are defined as above.

[00108] Compounds useful in the present invention include compounds of the formula:



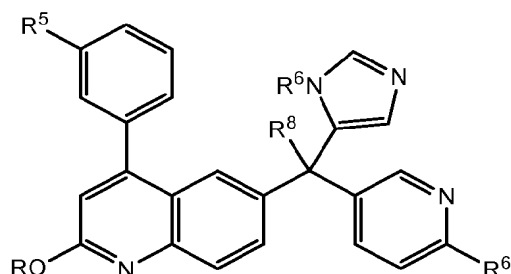
wherein R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are defined as above.

[00109] Compounds useful in the present invention include compounds of the formula:



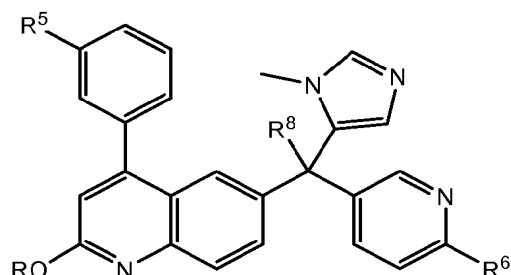
wherein R^2 , R^5 , R^6 , R^7 , and R^8 are defined as above.

[00110] Compounds useful in the present invention include compounds of the formula:



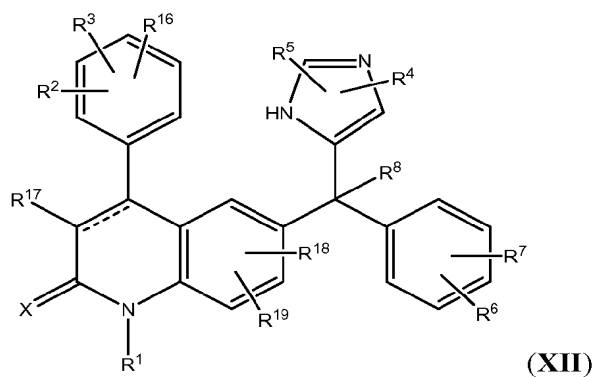
wherein R^5 , R^6 , and R^8 are defined as above.

[00111] Compounds useful in the present invention include compounds of the formula:



wherein R^5 , R^6 , and R^8 are defined as above.

[00112] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (XII):



(XII)

wherein

the dotted line represents an optional bond;

X is oxygen or sulfur;

R^1 is hydrogen, C_{1-12} alkyl, Ar^1 , Ar^2 C_{1-6} alkyl, quinolinyl C_{1-6} alkyl, pyridyl C_{1-6} alkyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyl, amino C_{1-6} alkyl, or a radical of formula $-Alk^1 -C(=O)-R^9$, $-Alk^1 -S(O)-R^9$ or $-Alk^1 -S(O)_2 -R^9$, wherein

Alk¹ is C₁₋₆ alkanediyl,

R⁹ is hydroxy, C₁₋₆ alkyl, C₁₋₆ alkyloxy, amino, C₁₋₈ alkylamino or C₁₋₈ alkylamino substituted with C₁₋₆ alkyloxycarbonyl;

R², R³, and R¹⁶ each independently are hydrogen, hydroxy, halo, cyano, C₁₋₆alkyl, C₁₋₆alkyloxy, hydroxyC₁₋₆alkyloxy, C₁₋₆alkyloxyC₁₋₆alkyloxy, aminoC₁₋₆alkyloxy, mono- or di(C₁₋₆alkyl)aminoC₁₋₆alkyloxy, Ar¹, Ar²C₁₋₆alkyl, Ar²oxy, Ar²C₁₋₆alkyloxy, hydroxycarbonyl, C₁₋₆alkyloxycarbonyl, trihalomethyl, trihalomethoxy, C₂₋₆alkenyl, 4,4-dimethyloxazolyl;

or when on adjacent positions R² and R³ taken together may form a bivalent radical of formula:



R⁴ and R⁵ each independently are hydrogen, halo, Ar¹, C₁₋₆alkyl, hydroxyC₁₋₆alkyl, C₁₋₆alkyloxyC₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylthio, amino, hydroxycarbonyl, C₁₋₆alkyloxycarbonyl, C₁₋₆alkylS(O)C₁₋₆alkyl or C₁₋₆alkylS(O)₂C₁₋₆alkyl;

R⁶ and R⁷ each independently are hydrogen, halo, cyano, C₁₋₆alkyl, C₁₋₆alkyloxy, Ar²oxy, trihalomethyl, C₁₋₆alkylthio, di(C₁₋₆alkyl)amino, or

when on adjacent positions R⁶ and R⁷ taken together may form a bivalent radical of formula:



R⁸ is hydrogen, C₁₋₆alkyl, cyano, hydroxycarbonyl, C₁₋₆alkyloxycarbonyl, C₁₋₆alkylcarbonylC₁₋₆alkyl, cyanoC₁₋₆alkyl, C₁₋₆alkyloxycarbonylC₁₋₆alkyl, carboxyC₁₋₆alkyl, hydroxyC₁₋₆alkyl, aminoC₁₋₆alkyl, mono- or di(C₁₋₆alkyl)aminoC₁₋₆alkyl, imidazolyl, haloC₁₋₆alkyl, C₁₋₆alkyloxyC₁₋₆alkyl, aminocarbonylC₁₋₆alkyl, or a radical of formula



wherein

R¹⁰ is hydrogen, C₁₋₆alkyl, C₁₋₆alkylcarbonyl, Ar¹, Ar²C₁₋₆alkyl, C₁₋₆alkyloxycarbonylC₁₋₆alkyl, a radical or formula -Alk²-OR¹³ or -Alk²-NR¹⁴R¹⁵;

R^{11} is hydrogen, C_{1-12} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{12} is hydrogen, C_{1-6} alkyl, C_{1-16} alkylcarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylaminocarbonyl, Ar^1 , Ar^2 C_{1-6} alkyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, a natural amino acid, Ar^1 carbonyl, Ar^2 C_{1-6} alkylcarbonyl, aminocarbonylcarbonyl, C_{1-6} alkyloxy C_{1-6} alkylcarbonyl, hydroxy, C_{1-6} alkyloxy, aminocarbonyl, di(C_{1-6} alkyl)amino C_{1-6} alkylcarbonyl, amino, C_{1-6} alkylamino, C_{1-6} alkylcarbonylamino, or a radical of formula $-Alk^2-OR^{13}$ or $-Alk^2-NR^{14}R^{15}$;

wherein

Alk^2 is C_{1-6} alkanediyl;

R^{13} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, hydroxy C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{14} is hydrogen, C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{15} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{17} is hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, Ar^1 ;

R^{18} is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy or halo;

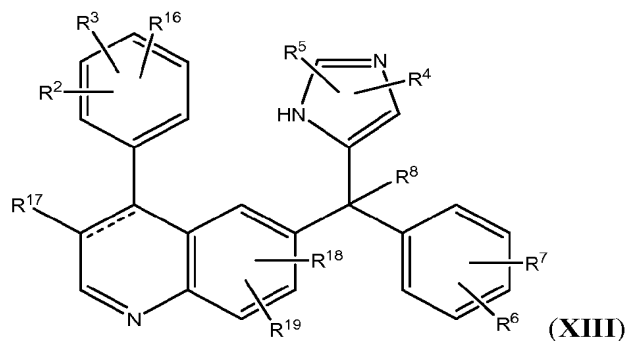
R^{19} is hydrogen or C_{1-6} alkyl;

Ar^1 is phenyl or phenyl substituted with C_{1-6} alkyl, hydroxy, amino, C_{1-6} alkyloxy, or halo; and

Ar^2 is phenyl or phenyl substituted with C_{1-6} alkyl, hydroxy, amino, C_{1-6} alkyloxy, or halo;

or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency.

[00113] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (XIII):



wherein

R^2 , R^3 , and R^{16} each independently are hydrogen, hydroxy, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxy, hydroxy C_{1-6} alkyloxy, C_{1-6} alkyloxy C_{1-6} alkyloxy, amino C_{1-6} alkyloxy, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyloxy, Ar^1 , Ar^2 C_{1-6} alkyl, Ar^2 oxy, Ar^2 C_{1-6} alkyloxy, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, trihalomethyl, trihalomethoxy, C_{2-6} alkenyl, 4,4-dimethyloxazolyl; or

when on adjacent positions R^2 and R^3 taken together may form a bivalent radical of formula



R^4 and R^5 each independently are hydrogen, halo, Ar^1 , C_{1-6} alkyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, C_{1-6} alkyloxy, C_{1-6} alkylthio, amino, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylS(O) C_{1-6} alkyl or C_{1-6} alkylS(O) $_2$ C_{1-6} alkyl;

R^6 and R^7 each independently are hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxy, Ar^2 oxy, trihalomethyl, C_{1-6} alkylthio, di (C_{1-6} alkyl) amino, or

when on adjacent positions R^6 and R^7 taken together may form a bivalent radical of formula



R^8 is hydrogen, C_{1-6} alkyl, cyano, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, cyano C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, carboxy C_{1-6} alkyl, hydroxy C_{1-6} alkyl, amino C_{1-6} alkyl, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyl, imidazolyl, halo C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, aminocarbonyl C_{1-6} alkyl, or a radical of formula



wherein

R^{10} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 , Ar^2 C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, a radical or formula $-Alk^2-OR^{13}$ or $-Alk^2-NR^{14}R^{15}$;

R^{11} is hydrogen, C_{1-12} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{12} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6}

alkylaminocarbonyl, Ar^1 , Ar^2 C_{1-6} alkyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, a natural amino acid, Ar^1 carbonyl, Ar^2 C_{1-6} alkylcarbonyl, aminocarbonylcarbonyl, C_{1-6} alkyloxy C_{1-6} alkylcarbonyl, hydroxy, C_{1-6} alkyloxy, aminocarbonyl, $\text{di}(\text{C}_{1-6}$ alkyl) amino C_{1-6} alkylcarbonyl, amino, C_{1-6} alkylamino, C_{1-6} alkylcarbonylamino, or a radical of formula - $\text{Alk}^2\text{-OR}^{13}$ or $\text{-Alk}^2\text{-NR}^{14}\text{R}^{15}$;

wherein Alk^2 is C_{1-6} alkanediyl;

R^{13} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, hydroxy C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{14} is hydrogen, C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{15} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 or Ar^2 C_{1-6} alkyl;

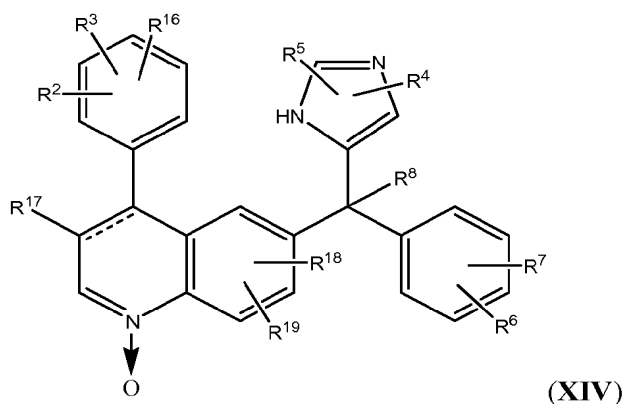
R^{17} is hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, Ar^1 ;

R^{18} is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy or halo;

R^{19} is hydrogen or C_{1-6} alkyl;

a stereoisomeric form or a pharmaceutically acceptable acid or base addition salt form thereof, at a therapeutically effective dose and frequency.

[00114] In another embodiment the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (XIV):



wherein R^2 , R^3 , and R^{16} each independently are hydrogen, hydroxy, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxy, hydroxy C_{1-6} alkyloxy, C_{1-6} alkyloxy C_{1-6} alkyloxy, amino C_{1-6} alkyloxy, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyloxy, Ar^1 , Ar^2 C_{1-6} alkyl, Ar^2 oxy, Ar^2 C_{1-6} alkyloxy, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, trihalomethyl, trihalomethoxy, C_{2-6} alkenyl, 4,4-dimethyloxazolyl; or

when on adjacent positions R^2 and R^3 taken together may form a bivalent radical of formula:

- O-CH₂-O- (a-1),
- O-CH₂-CH₂-O- (a-2),
- O-CH=CH- (a-3),
- O-CH₂-CH₂- (a-4),
- O-CH₂-CH₂-CH₂- (a-5), or
- CH=CH-CH=CH- (a-6);

R⁴ and R⁵ each independently are hydrogen, halo, Ar¹, C₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkyloxy, C₁₋₆ alkylthio, amino, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl;

R⁶ and R⁷ each independently are hydrogen, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxy, Ar² oxy, trihalomethyl, C₁₋₆ alkylthio, di (C₁₋₆ alkyl) amino, or

when on adjacent positions R⁶ and R⁷ taken together may form a bivalent radical of formula

- O-CH₂-O- (c-1), or
- CH=CH-CH=CH- (c-2);

R⁸ is hydrogen, C₁₋₆alkyl, cyano, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylcarbonylC₁₋₆alkyl, cyanoC₁₋₆alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆alkyl, carboxyC₁₋₆ alkyl, hydroxyC₁₋₆alkyl, aminoC₁₋₆ alkyl, mono- or di (C₁₋₆ alkyl)aminoC₁₋₆alkyl, imidazolyl, haloC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, aminocarbonylC₁₋₆ alkyl, or a radical of formula

- O-R¹⁰ (b- 1),
- S-R¹⁰ (b- 2),
- N-R¹¹R¹² (b- 3),

wherein

R¹⁰ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, Ar¹, Ar² C₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, a radical or formula -Alk² -OR¹³ or -Alk² -NR¹⁴ R¹⁵ ;

R¹¹ is hydrogen, C₁₋₁₂ alkyl, Ar¹ or Ar² C₁₋₆ alkyl;

R¹² is hydrogen, C₁₋₆ alkyl, C₁₋₁₆ alkylcarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylaminocarbonyl, Ar¹, Ar² C₁₋₆ alkyl, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, a natural amino acid, Ar¹ carbonyl, Ar² C₁₋₆ alkylcarbonyl, aminocarbonylcarbonyl, C₁₋₆ alkyloxyC₁₋₆ alkylcarbonyl, hydroxy, C₁₋₆ alkyloxy, aminocarbonyl, di(C₁₋₆ alkyl)aminoC₁₋₆ alkylcarbonyl, amino, C₁₋₆ alkylamino, C₁₋₆ alkylcarbonylamino, or a radical of formula -Alk² -OR¹³ or -Alk² -NR¹⁴ R¹⁵ ;

wherein

Alk² is C₁₋₆ alkanediyl;

R^{13} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, hydroxy C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{14} is hydrogen, C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{15} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 or Ar^2 C_{1-6} alkyl;

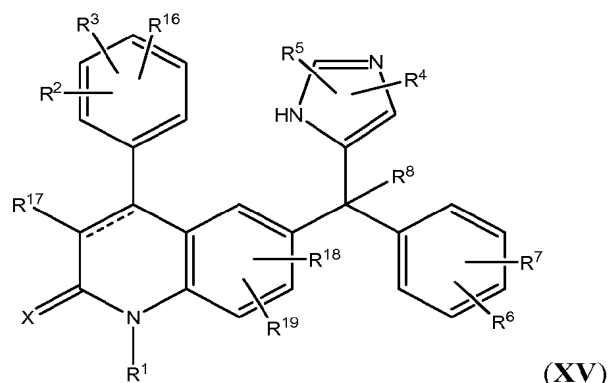
R^{17} is hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, Ar^1 ;

R^{18} is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy or halo;

R^{19} is hydrogen or C_{1-6} alkyl;

or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency.

[00115] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (XV):



or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof,

wherein the dotted line represents an optional bond;

X is oxygen or sulfur;

R^1 is hydrogen, C_{1-12} alkyl, Ar^1 , Ar^2 C_{1-6} alkyl, quinolinyl C_{1-6} -alkyl, pyridyl C_{1-6} alkyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyl, amino C_{1-6} alkyl, or a radical of formula $-Alk^1-C(=O)-R^9$, $-Alk^1-S(O)-R^9$ or $-Alk^1-S(O)_2--R^9$, wherein Alk^1 is C_{1-6} alkanediyl,

R^9 is hydroxy, C_{1-6} alkyl, C_{1-6} alkyloxy, amino, C_{1-8} alkylamino or C_{1-8} alkylamino substituted with C_{1-6} alkyloxycarbonyl;

R^2 , R^3 , and R^{16} each independently are hydrogen, hydroxy, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxy, hydroxy C_{1-6} alkyloxy, C_{1-6} alkyloxy C_{1-6} alkyloxy, amino C_{1-6} alkyloxy, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyloxy, Ar^1 , Ar^2 C_{1-6} alkyl, Ar^2 oxy, Ar^2 C_{1-6} alkyloxy,

hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, trihalomethyl, trihalomethoxy, C₂₋₆ alkenyl, 4,4-dimethyloxazolyl; or

when on adjacent positions R² and R³ taken together may form a bivalent radical of formula



R⁴ is hydrogen or C₁₋₆ alkyl;

R⁵ is hydrogen;

R⁶ and R⁷ each independently are hydrogen, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxy, Ar² oxy, trihalomethyl, C₁₋₆ alkylthio, di(C₁₋₆ alkyl)amino, or

when on adjacent positions R⁶ and R⁷ taken together may form a bivalent radical of formula:



R⁸ is hydrogen, C₁₋₆ alkyl, cyano, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkyl, cyanoC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, carboxyC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, aminoC₁₋₆ alkyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl, imidazolyl, haloC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, aminocarbonylC₁₋₆ alkyl, or a radical of formula:



wherein

R¹⁰ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, Ar¹, Ar² C₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, a radical or formula --Alk² --OR¹³ or --Alk² --NR¹⁴ R¹⁵ ;

R¹¹ is hydrogen, C₁₋₁₂ alkyl, Ar¹ or Ar² C₁₋₆ alkyl;

R¹² is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylaminocarbonyl, Ar¹, Ar² C₁₋₆ alkyl, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, a natural amino acid, Ar¹ carbonyl, Ar² C₁₋₆ alkylcarbonyl, aminocarbonylcarbonyl, C₁₋₆ alkyloxyC₁₋₆ alkylcarbonyl, hydroxy, C₁₋₆ alkyloxy, aminocarbonyl, di(C₁₋₆ alkyl) aminoC₁₋₆ alkylcarbonyl, amino, C₁₋₆ alkylamino, C₁₋₆ alkylcarbonylamino, or a radical of formula -Alk²-OR¹³ or -Alk²-NR¹⁴ R¹⁵ ;

wherein Alk² is C₁₋₆ alkanediyl;

R^{13} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, hydroxy C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{14} is hydrogen, C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{15} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{17} is hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, Ar^1 ;

R^{18} is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy or halo;

R^{19} is hydrogen or C_{1-6} alkyl;

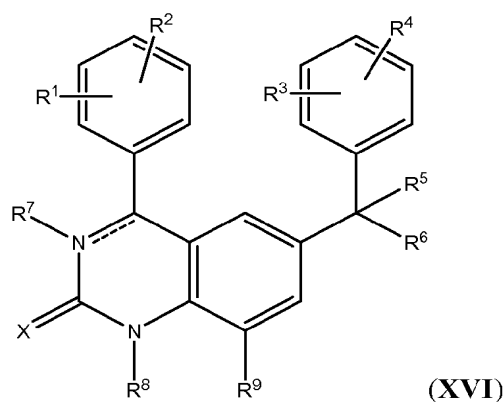
Ar^1 is phenyl or phenyl substituted with C_{1-6} alkyl, hydroxy, amino, C_{1-6} alkyloxy or halo; and

Ar^2 is phenyl or phenyl substituted with C_{1-6} alkyl, hydroxy, amino, C_{1-6} alkyloxy or halo;

or a stereoisomeric form or a pharmaceutically acceptable acid or base addition salt form thereof, at a therapeutically effective dose and frequency.

[00116] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor compound that is an enantiomer of 6-(amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl)-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone having an α_D^{20} value of $+22.86^\circ$ ($c=49.22$ mg/5 ml, methanol) or a pharmaceutically acceptable salt thereof, at a therapeutically acceptable dose and frequency.

[00117] In another embodiment the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (XVI):



wherein

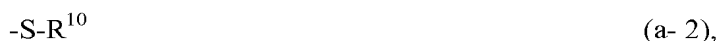
the dotted line represents an optional bond;

X is oxygen or sulfur;

R^1 and R^2 each independently are hydrogen, hydroxy, halo, cyano, C_{1-6} alkyl, trihalomethyl, trihalomethoxy, C_{2-6} alkenyl, C_{1-6} alkyloxy, hydroxy C_{1-6} alkyloxy, C_{1-6} alkyloxy C_{1-6} alkyloxy, C_{1-6} alkyloxycarbonyl, amino C_{1-6} alkyloxy, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyloxy, Ar^1 , Ar^1 C_{1-6} alkyl, Ar^1 oxy, Ar^1 C_{1-6} alkyloxy;

R^3 and R^4 each independently are hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxy, Ar^1 oxy, C_{1-6} alkylthio, di(C_{1-6} alkyl)amino, trihalomethyl or trihalomethoxy;

R^5 is hydrogen, halo, C_{1-6} alkyl, cyano, halo C_{1-6} alkyl, hydroxy C_{1-6} alkyl, cyano C_{1-6} alkyl, amino C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, C_{1-6} alkylthio C_{1-6} alkyl, aminocarbonyl C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyl, Ar^1 , Ar^1 C_{1-6} alkyloxy C_{1-6} alkyl; or a radical of formula:



wherein

R^{10} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 , Ar^1 C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, or a radical of formula $--Alk--OR^{13}$ or $--Alk--NR^{14} R^{15}$;

R^{11} is hydrogen, C_{1-6} alkyl, Ar^1 or Ar^1 C_{1-6} alkyl;

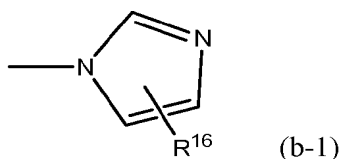
R^{12} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylaminocarbonyl, Ar^1 , Ar^1 C_{1-6} alkyl, C_{1-6} alkylcarbonyl- C_{1-6} alkyl, Ar^1 carbonyl, Ar^1 C_{1-6} alkylcarbonyl, aminocarbonylcarbonyl, C_{1-6} alkyloxy C_{1-6} alkylcarbonyl, hydroxy, C_{1-6} alkyloxy, aminocarbonyl, di(C_{1-6} alkyl)amino C_{1-6} alkylcarbonyl, amino, C_{1-6} alkylamino, C_{1-6} alkylcarbonylamino, or a radical or formula $--Alk--OR^{13}$ or $--Alk--NR^{14} R^{15}$; wherein Alk is C_{1-6} alkanediyl;

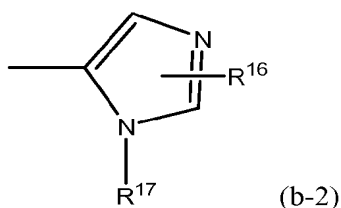
R^{13} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, hydroxy C_{1-6} alkyl, Ar^1 or Ar^1 C_{1-6} alkyl;

R^{14} is hydrogen, C_{1-6} alkyl, Ar^1 or Ar^1 C_{1-6} alkyl;

R^{15} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 or Ar^1 C_{1-6} alkyl;

R^6 is a radical of formula:





wherein

R^{16} is hydrogen, halo, Ar^1 , C_{1-6} alkyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, C_{1-6} alkyloxy, C_{1-6} alkylthio, amino, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylthio C_{1-6} alkyl, C_{1-6} alkylS(O) C_{1-6} alkyl or C_{1-6} alkylS(O) $_2$ C_{1-6} alkyl;

R^{17} is hydrogen, C_{1-6} alkyl or di(C_{1-4} alkyl)aminosulfonyl;

R^7 is hydrogen or C_{1-6} alkyl provided that the dotted line does not represent a bond;

R^8 is hydrogen, C_{1-6} alkyl or Ar^2 CH_2 or Het^1 CH_2 ;

R^9 is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy or halo; or

R^8 and R^9 taken together to form a bivalent radical of formula:

-CH=CH- (c-1)

-CH₂-CH₂- (c-2)

-CH₂-CH₂-CH₂- (c-3)

-CH₂-O- (c-4), or

-CH₂-CH₂-O- (c-5)

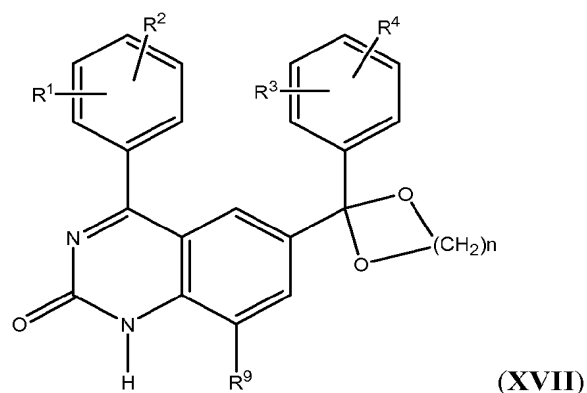
Ar^1 is phenyl; or phenyl substituted with 1 or 2 substituents each independently selected from halo, C_{1-6} alkyl, C_{1-6} alkyloxy or trifluoromethyl;

Ar^2 is phenyl; or phenyl substituted with 1 or 2 substituents each independently selected from halo, C_{1-6} alkyl, C_{1-6} alkyloxy or trifluoromethyl; and

Het^1 is pyridinyl; pyridinyl substituted with 1 or 2 substituents each independently selected from halo, C_{1-6} alkyl, C_{1-6} alkyloxy or trifluoromethyl;

or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency.

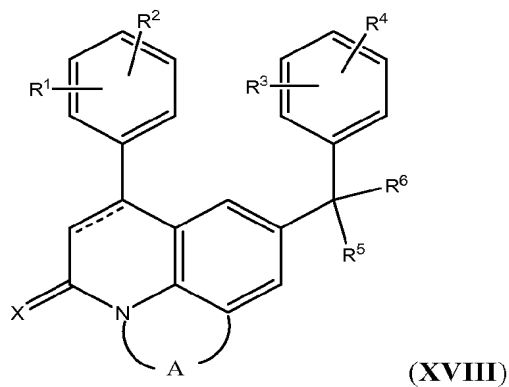
[00118] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (XVII):



wherein

n is 2 or 3; and R^1 , R^2 , R^3 , R^4 , and R^9 are as defined previously,
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency.

[00119] In another embodiment the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (XVIII):



wherein

the dotted line represents an optional bond;

X is oxygen or sulfur;

-A- is a bivalent radical of formula:

- | | |
|--|--------|
| -CH=CH- | (a-1), |
| -CH ₂ -CH ₂ - | (a-2), |
| -CH ₂ -CH ₂ -CH ₂ - | (a-3), |
| -CH ₂ -O- | (a-4), |
| -CH ₂ -CH ₂ -O- | (a-5), |
| -CH ₂ -S- | (a-6), |

- CH₂-CH₂-S- (a-7),
 -CH=N- (a-8),
 -N=N- (a-9), or
 -CO-NH- (a-10);

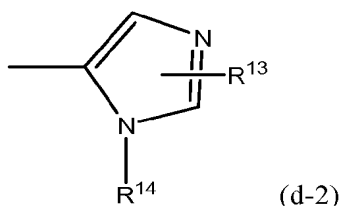
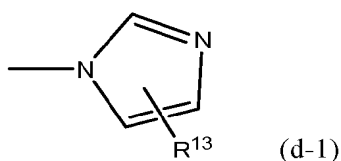
R¹ and R² each independently are hydrogen, hydroxy, halo, cyano, C₁₋₆ alkyl, trihalomethyl, trihalomethoxy, C₂₋₆ alkenyl, C¹⁻⁶ alkyloxy, hydroxy C₁₋₆ alkyloxy, C₁₋₆ alkyloxyC₁₋₆ alkyloxy, C₁₋₆ alkyloxycarbonyl, aminoC₁₋₆ alkyloxy, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyloxy, Ar², Ar² --C₁₋₆ alkyl, Ar² -oxy, Ar² --C₁₋₆ alkyloxy; or when on adjacent positions R¹ and R² taken together may form a bivalent radical of formula:

- O-CH₂-O- (b-1),
 -O-CH₂-CH₂-O- (b-2),
 -O-CH=CH- (b-3),
 -O-CH₂-CH₂- (b-4),
 -O-CH₂-CH₂-CH₂- (b-5), or
 -CH=CH-CH=CH- (b-6);

R³ and R⁴ each independently are hydrogen, halo, cyano, C₁₋₆alkyl, C₁₋₆alkoxy, Ar³-oxy, C₁₋₆alkylthio, di(C₁₋₆alkyl)amino, trihalomethyl, trihalomethoxy, or when on adjacent positions R³ and R⁴ taken together may form a bivalent radical of formula:

- O-CH₂-O- (c-1),
 -O-CH₂-CH₂-O- (c-2), or
 -CH=CH-CH=CH- (c-3);

R⁵ is a radical of formula:



wherein R¹³ is hydrogen, halo, Ar⁴, C₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkyloxy, C₁₋₆ alkylthio, amino, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl; R¹⁴ is hydrogen, C₁₋₆ alkyl or di(C₁₋₄ alkyl)aminosulfonyl;

R^6 is hydrogen, hydroxy, halo, C_{1-6} alkyl, cyano, halo C_{1-6} alkyl, hydroxy C_{1-6} alkyl, cyano C_{1-6} alkyl, amino C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, C_{1-6} alkylthio C_{1-6} alkyl, aminocarbonyl- C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyl, Ar^5 , Ar^5 -- C_{1-6} alkyloxy C_{1-6} alkyl; or a radical of formula



wherein

R^7 is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^6 , Ar^6 -- C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, or a radical of formula --Alk--OR¹⁰ or --Alk--NR¹¹ R¹²;

R^8 is hydrogen, C_{1-6} alkyl, Ar^7 or Ar^7 -- C_{1-6} alkyl;

R^9 is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylaminocarbonyl, Ar^8 , Ar^8 -- C_{1-6} alkyl, C_{1-6} alkylcarbonyl- C_{1-6} alkyl, Ar^8 --carbonyl, Ar^8 -- C_{1-6} alkylcarbonyl, aminocarbonylcarbonyl, C_{1-6} alkyloxy C_{1-6} alkylcarbonyl, hydroxy, C_{1-6} alkyloxy, aminocarbonyl, di(C_{1-6} alkyl)amino C_{1-6} alkylcarbonyl, amino, C_{1-6} alkylamino, C_{1-6} alkylcarbonylamino, or a radical or formula --Alk--OR¹⁰ or --Alk--NR¹¹ R¹²;

wherein Alk is C_{1-6} alkanediyl;

R^{10} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, hydroxy C_{1-6} alkyl, Ar^9 or Ar^9 -- C_{1-6} alkyl;

R^{11} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^{10} or Ar^{10} -- C_{1-6} alkyl;

R^{12} is hydrogen, C_{1-6} alkyl, Ar^{11} or Ar^{11} -- C_{1-6} alkyl; and

Ar^1 to Ar^{11} are each independently selected from phenyl; or phenyl substituted with halo, C_{1-6} alkyl, C_{1-6} alkyloxy or trifluoromethyl,

or a stereoisomeric form or a pharmaceutically acceptable acid or base addition salt form thereof, at a therapeutically effective dose and frequency.

[00120] In one embodiment, the dotted line represents an optional bond;

X is O or S;

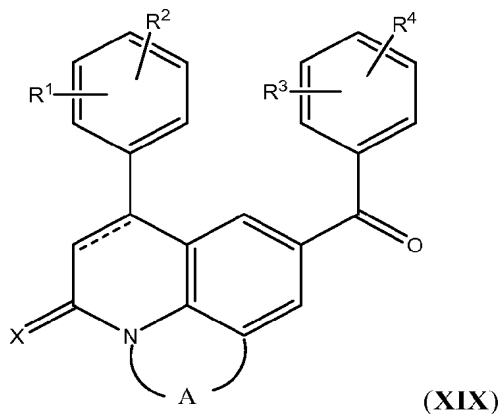
R^1 and R^2 are each independently selected from hydrogen, halo, C_{1-6} alkyl, C_{1-6} alkyloxy, trihalomethyl or trihalomethoxy;

R^3 and R^4 are each independently selected from hydrogen, halo, C_{1-6} alkyl, C^{1-6} alkyloxy, trihalomethyl or trihalomethoxy;

R^5 a radical of formula (d-1) wherein R^{13} is hydrogen or R^5 is a radical of formula (d-2) wherein R^{13} is hydrogen or C_{1-6} alkyl and R^{14} is hydrogen or C_{1-6} alkyl; and

R⁶ is hydrogen, hydroxy, haloC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, cyanoC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, or a radical of formula -NR⁸ R⁹ wherein R⁸ is hydrogen or C₁₋₆ alkyl and R⁹ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkyloxy or C₁₋₆ alkyloxyC₁₋₆ alkylcarbonyl.

[00121] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (XIX):

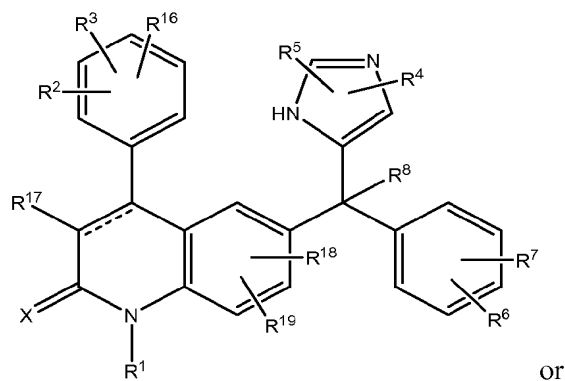


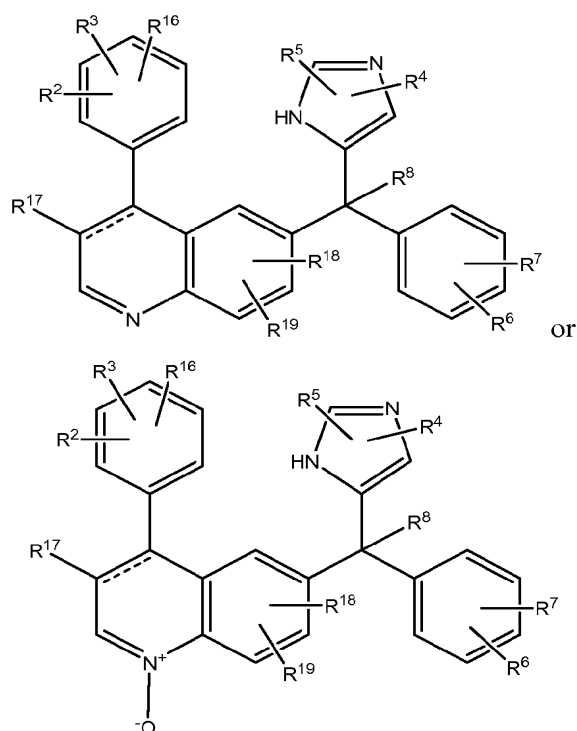
wherein

the dotted line represents an optional bond; wherein X, -A-, R¹, R², R³, and R⁴ are as defined previously;

or a stereoisomeric form or a pharmaceutically acceptable acid or base addition salt form thereof, at a therapeutically effective dose and frequency.

[00122] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:





wherein

the dotted line represents an optional bond;

X is oxygen or sulfur;

R¹ is hydrogen, C₁₋₁₂alkyl, Ar¹, Ar² C₁₋₆alkyl, quinolinylC₁₋₆alkyl, pyridylC₁₋₆alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆alkyl, mono- or di(C₁₋₆ alkyl) aminoC₁₋₆alkyl, aminoC₁₋₆alkyl, or a radical of formula -Alk¹-C(=O)-R⁹, -Alk¹-S(O)-R⁹ or -Alk¹-S(O)₂-R⁹,

wherein

Alk¹ is C₁₋₆ alkanediyl,

R⁹ is hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, amino, C₁₋₈alkylamino, or C₁₋₈alkylamino substituted with C₁₋₆alkyloxycarbonyl;

R², R³, and R¹⁶ each independently are hydrogen, hydroxy, halo, cyano, C₁₋₆alkyl, C₁₋₆alkyloxy, hydroxyC₁₋₆alkyloxy, C₁₋₆alkyloxyC₁₋₆alkyloxy, aminoC₁₋₆alkyloxy, mono- or di(C₁₋₆alkyl)aminoC₁₋₆alkyloxy, Ar¹, Ar²C₁₋₆alkyl, Ar² oxy, Ar²C₁₋₆alkyloxy, hydroxycarbonyl, C₁₋₆alkyloxycarbonyl, trihalomethyl, trihalomethoxy, C₂₋₆alkenyl, 4,4-dimethyloxazolyl; or

when on adjacent positions R² and R³ taken together may form a bivalent radical of formula:





R^4 and R^5 each independently are hydrogen, halo, Ar^1 , C_{1-6} alkyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, C_{1-6} alkyloxy, C_{1-6} alkylthio, amino, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylS (O) C_{1-6} alkyl or C_{1-6} alkylS (O)₂ C_{1-6} alkyl;

R^6 and R^7 each independently are hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxy, Ar^2 oxy, trihalomethyl, C_{1-6} alkylthio, di (C_{1-6} alkyl) amino, or when on adjacent positions R^6 and R^7 taken together may form a bivalent radical of formula



R^8 is hydrogen, C_{1-6} alkyl, cyano, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, cyanoc C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, carboxy C_{1-6} alkyl, hydroxy C_{1-6} alkyl, amino C_{1-6} alkyl, mono- or di (C_{1-6} alkyl)-amino C_{1-6} alkyl, imidazolyl, halo C_{1-6} alkyl, C_{1-6} alkyloxy- C_{1-6} alkyl, aminocarbonyl C_{1-6} alkyl, or a radical of formula



wherein

R^{10} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 , Ar^2 C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, a radical or formula $\text{-Alk}^2\text{-OR}^{13}$ or $\text{-Alk}^2\text{-NR}^{14} \text{ R}^{15}$;

R^{11} is hydrogen, C_{1-12} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{12} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylaminocarbonyl, Ar^1 , Ar^2 C_{1-6} alkyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, a natural amino acid, Ar^1 carbonyl, Ar^2 C_{1-6} alkylcarbonyl, aminocarbonylcarbonyl, C_{1-6} alkyloxy C_{1-6} alkylcarbonyl, hydroxy, C_{1-6} alkyloxy, aminocarbonyl, di(C_{1-6} alkyl)amino C_{1-6} alkylcarbonyl, amino, C_{1-6} alkylamino, C_{1-6} alkylcarbonylamino, or a radical of formula $\text{-Alk}^2\text{-OR}^{13}$ or $\text{-Alk}^2\text{-NR}^{14} \text{ R}^{15}$;

wherein

Alk^2 is C_{1-6} alkanediyl;

R^{13} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, hydroxy C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{14} is hydrogen, C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{15} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{17} is hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} -alkyloxycarbonyl, Ar^1 ;

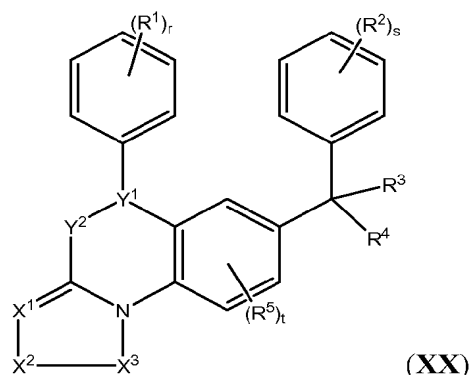
R^{18} is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy or halo;

R^{19} is hydrogen or C_{1-6} alkyl;

Ar^1 is phenyl or phenyl substituted with C_{1-6} alkyl, hydroxy, amino, C_{1-6} alkyloxy or halo; and

Ar^2 is phenyl or phenyl substituted with C_{1-6} alkyl, hydroxy, amino, C_{1-6} alkyloxy or halo; or a stereoisomeric form or a pharmaceutically acceptable acid or base addition salt form thereof, at a therapeutically effective dose and frequency.

[00123] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:



wherein

$=X^1-X^2-X^3-$ is a trivalent radical of formula

$=N-CR^6=CR^7-$ (x-1),

$=N-N=CR^6-$ (x-2),

$=N-NH-C(=O)-$ (x-3),

$=N-N=N-$ (x-4),

$=N-CR^6=N-$ (x-5),

$=CR^6-CR^7=CR^8-$ (x-6),

$=CR^6-N=CR^7-$ (x-7),

$=CR^6-NH-C(=O)-$ (x-8), or

$=CR^6-N=N-$ (x-9);

wherein each R^6 , R^7 and R^8 are independently hydrogen, C_{1-4} alkyl, hydroxy, C_{1-4} alkyloxy, aryloxy, C_{1-4} alkyloxycarbonyl, hydroxy C_{1-6} alkyl, C_{1-4} alkyloxy C_{1-4} alkyl, mono- or di(C_{1-6} alkyl)amino C_{1-4} alkyl, cyano, amino, thio, C_{1-4} alkylthio, arylthio or aryl;

$>Y^1-Y^2$ is a trivalent radical of formula



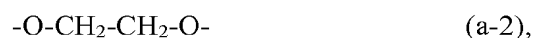
wherein each R^9 independently is hydrogen, halo, halocarbonyl, aminocarbonyl, hydroxy C_{1-4} alkyl, cyano, carboxyl, C_{1-4} alkyl, C_{1-4} alkyloxy, C_{1-4} alkyloxy C_{1-4} alkyl, C_{1-4} alkyloxycarbonyl, mono- or di(C_{1-6} alkyl)amino, mono- or di(C_{1-4} alkyl)amino C_{1-4} alkyl, or aryl;

r and s are each independently 0, 1, 2, 3, 4 or 5;

t is 0, 1, 2 or 3;

each R^1 and R^2 are independently hydroxy, halo, cyano, C_{1-6} alkyl, trihalomethyl, trihalomethoxy, C_{2-6} alkenyl, C_{1-6} alkyloxy, hydroxy C_{1-6} alkyloxy, C_{1-6} alkylthio, C_{1-6} alkyloxy C_{1-6} alkyloxy, C_{1-6} alkyloxycarbonyl, amino C_{1-6} alkyloxy, mono- or di(C_{1-6} alkyl)amino, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyloxy, aryl, aryl C_{1-6} alkyl, aryloxy or aryl C_{1-6} alkyloxy, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, aminocarbonyl, amino C_{1-6} alkyl, mono- or di(C_{1-6} alkyl)aminocarbonyl, or mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyl; or

two R^1 or R^2 substituents adjacent to one another on the phenyl ring independently form together a bivalent radical of formula:



R^3 is hydrogen, halo, C_{1-6} alkyl, cyano, halo C_{1-6} alkyl, hydroxy C_{1-6} alkyl, cyano C_{1-6} alkyl, amino C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, C_{1-6} alkylthio C_{1-6} alkyl, aminocarbonyl, C_{1-6} alkyl, hydroxycarbonyl, hydroxycarbonyl C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, aryl, aryl C_{1-6} alkyloxy C_{1-6} alkyl, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyl; or a radical of formula:



wherein R^{10} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, aryl, aryl C_{1-6} alkyl, C_{1-6}

alkyloxycarbonyl C₁₋₆ alkyl, or a radical of formula -Alk--OR¹³ or -Alk--NR¹⁴ R¹⁵;

R¹¹ is hydrogen, C₁₋₆ alkyl, aryl or arylC₁₋₆ alkyl;

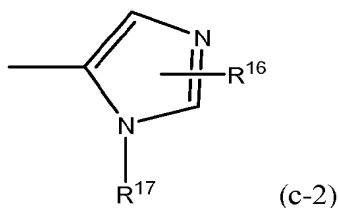
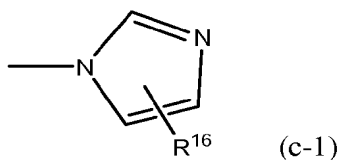
R¹² is hydrogen, C₁₋₆ alkyl, aryl, hydroxy, amino, C₁₋₆ alkyloxy, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, arylC₁₋₆ alkyl, C₁₋₆ alkylcarbonylamino, mono- or di(C₁₋₆ alkyl)amino, C₁₋₆ alkylcarbonyl, aminocarbonyl, arylcarbonyl, haloC₁₋₆ alkylcarbonyl, arylC₁₋₆ alkylcarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkyloxyC₁₋₆ alkylcarbonyl, mono- or di(C₁₋₆ alkyl)aminocarbonyl wherein the alkyl moiety may optionally be substituted by one or more substituents independently selected from aryl or C₁₋₃ alkyloxycarbonyl, aminocarbonylcarbonyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkylcarbonyl, or a radical of formula -Alk--OR¹³ or -Alk--NR¹⁴ R¹⁵; wherein Alk is C₁₋₆ alkanediyl;

R¹³ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, hydroxyC₁₋₆ alkyl, aryl or arylC₁₋₆ alkyl;

R¹⁴ is hydrogen, C₁₋₆ alkyl, aryl or arylC₁₋₆ alkyl;

R¹⁵ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, aryl or arylC₁₋₆ alkyl;

R⁴ is a radical of formula



wherein R¹⁶ is hydrogen, halo, aryl, C₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkyloxy, C₁₋₆ alkylthio, amino, mono- or di(C₁₋₄ alkyl)amino, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylthioC₁₋₆ alkyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆alkylS(O)₂ C₁₋₆alkyl;

R¹⁷ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, arylC₁₋₆ alkyl, trifluoromethyl or di(C₁₋₄ alkyl)aminosulfonyl;

R⁵ is C₁₋₆ alkyl, C₁₋₆ alkyloxy or halo; aryl is phenyl, naphthalenyl or phenyl substituted with one or more substituents each independently selected from halo, C₁₋₆ alkyl, C₁₋₆ alkyloxy or trifluoromethyl; with the proviso that that when R¹⁶ is bound to one of the nitrogen atoms in the imidazole ring of formula (c-1) or (c-2), R¹⁶ is hydrogen, aryl, C₁₋₆

alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl;

or a stereoisomeric form or a pharmaceutically acceptable acid or base addition salt form thereof, at a therapeutically effective dose and frequency.

[00124] In one embodiment, each R¹ and R² are independently hydroxy, halo, cyano, C₁₋₆ alkyl, trihalomethyl, trihalomethoxy, C₂₋₆ alkenyl, C₁₋₆ alkyloxy, hydroxyC₁₋₆ alkyloxy, C₁₋₆ alkylthio, C₁₋₆ alkyloxyC₁₋₆ alkyloxy, C₁₋₆ alkyloxycarbonyl, aminoC₁₋₆ alkyloxy, mono- or di(C₁₋₆ alkyl)amino, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyloxy, aryl, arylC₁₋₆ alkyl, aryloxy or arylC₁₋₆ alkyloxy, hydroxycarbonyl, or C₁₋₆ alkyloxycarbonyl; or

two R¹ or R² substituents adjacent to one another on the phenyl ring independently form together a bivalent radical of formula

-O-CH₂-O- (a-1),

-O-CH₂-CH₂-O- (a-2),

-O=CH=CH- (a-3),

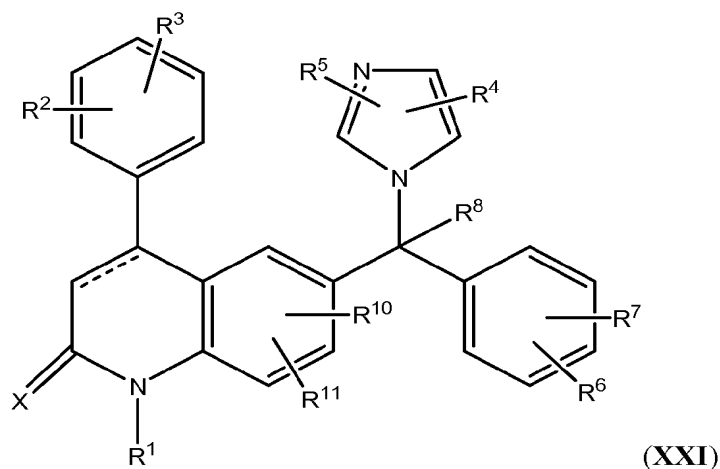
-O-CH₂-CH₂- (a-4),

-O-CH₂-CH₂-CH₂- (a-5), or

-CH=CH-CH=CH- (a-6);

R¹⁷ is hydrogen, C₁₋₆ alkyl, trifluoromethyl or di(C₁₋₆ alkyl)aminosulfonyl; with the proviso that that when R¹⁶ is bound to one of the nitrogen atoms in the imidazole ring of formula (c-1), R¹⁶ is hydrogen, aryl, C₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl.

[00125] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:



wherein

the dotted line represents an optional bond;

X is oxygen or sulfur;

R¹ is hydrogen, C₁₋₁₂ alkyl, Ar¹, Ar² C₁₋₆ alkyl, quinolinylC₁₋₆ alkyl, pyridylC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl, aminoC₁₋₆ alkyl, or a radical of formula -Alk¹-C(=O)-R⁹, -Alk¹-S(O)-R⁹ or -Alk¹-S(O)₂-R⁹, wherein Alk¹ is C₁₋₆ alkanediyl,

R⁹ is hydroxy, C₁₋₆ alkyl, C₁₋₆ alkyloxy, amino, C₁₋₈ alkylamino or C₁₋₈ alkylamino substituted with C₁₋₆ alkyloxycarbonyl;

R² and R³ each independently are hydrogen, hydroxy, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxy, hydroxyC₁₋₆ alkyloxy, C₁₋₆ alkyloxyC₁₋₆ alkyloxy, aminoC₁₋₆ alkyloxy, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyloxy, Ar¹, Ar² C₁₋₆ alkyl, Ar² oxy, Ar² C₁₋₆ alkyloxy, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, trihalomethyl, trihalomethoxy, C₂₋₆ alkenyl; or when on adjacent positions R² and R³ taken together may form a bivalent radical of formula

-O-CH₂-O- (a-1),

-O-CH₂-CH₂-O- (a-2),

-O-CH=CH- (a-3),

-O-CH₂-CH₂- (a-4),

-O-CH₂-CH₂-CH₂- (a-5), or

-CH=CH-CH=CH- (a-6);

R⁴ and R⁵ each independently are hydrogen, Ar¹, C₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkyloxy, C₁₋₆ alkylthio, amino, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl;

R⁶ and R⁷ each independently are hydrogen, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxy or Ar² oxy;

R⁸ is hydrogen, C₁₋₆ alkyl, cyano, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, cyanoC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, hydroxycarbonylC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, aminoC₁₋₆ alkyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl, haloC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, aminocarbonylC₁₋₆ alkyl, Ar¹, Ar² C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkylthioC₁₋₆ alkyl;

R¹⁰ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkyloxy or halo;

R¹¹ is hydrogen or C₁₋₆ alkyl;

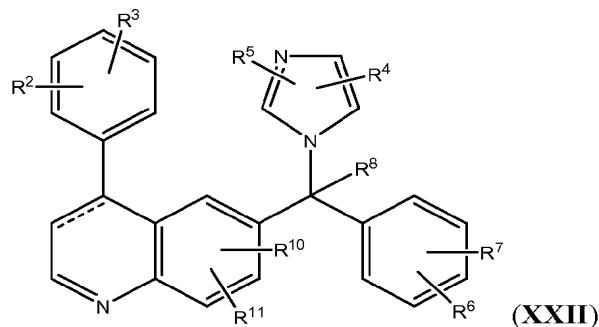
Ar¹ is phenyl or phenyl substituted with C₁₋₆ alkyl, hydroxy, amino, C₁₋₆ alkyloxy or halo; and

Ar² is phenyl or phenyl substituted with C₁₋₆ alkyl, hydroxy, amino, C₁₋₆ alkyloxy or

halo,

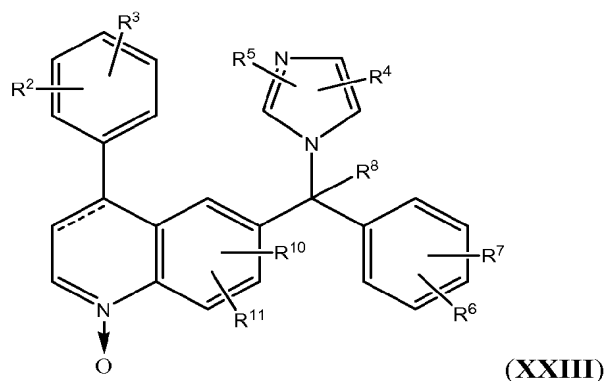
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency.

[00126] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (XXII):



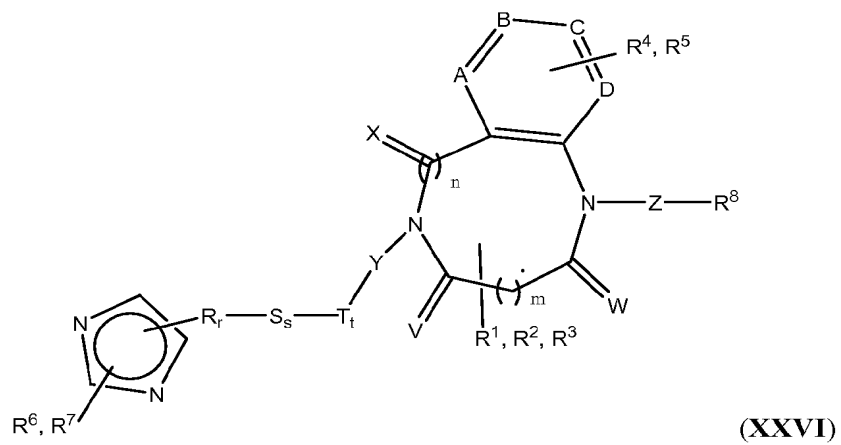
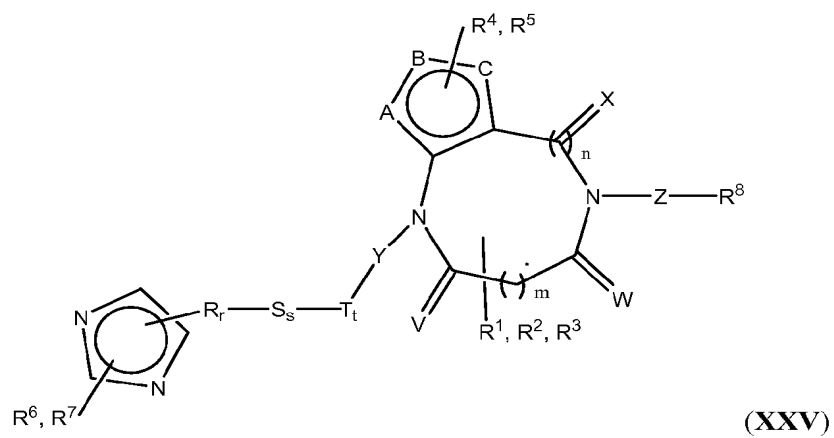
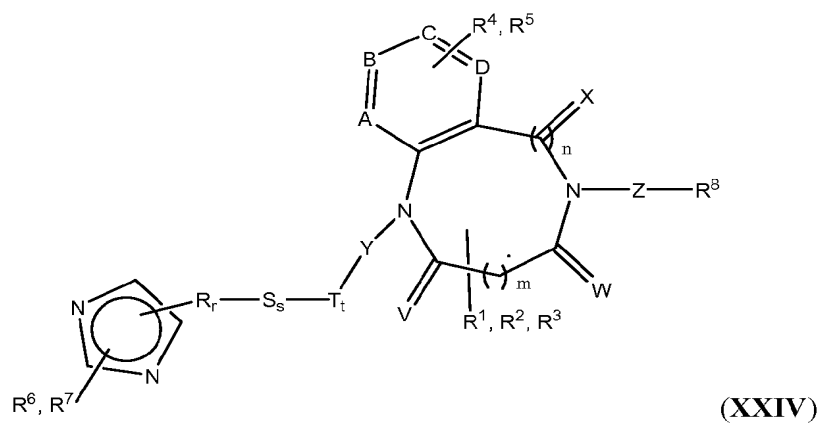
wherein the radicals R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₁₀, and R₁₁ are as defined above, or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency.

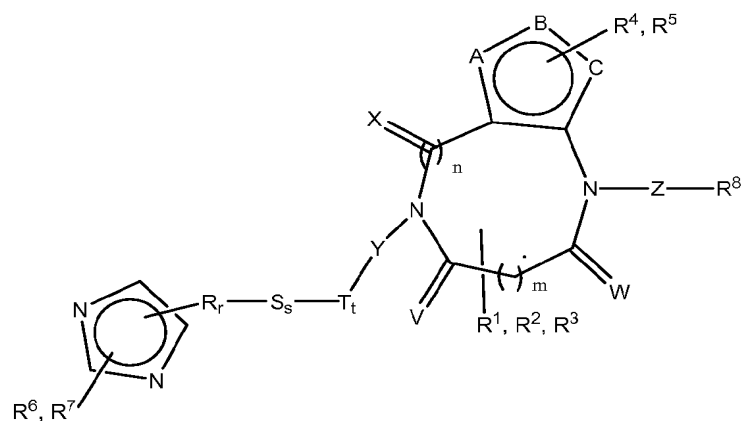
[00127] In another embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula (XXIII):



wherein the radicals R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₁₀, and R₁₁ are as defined above, or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency.

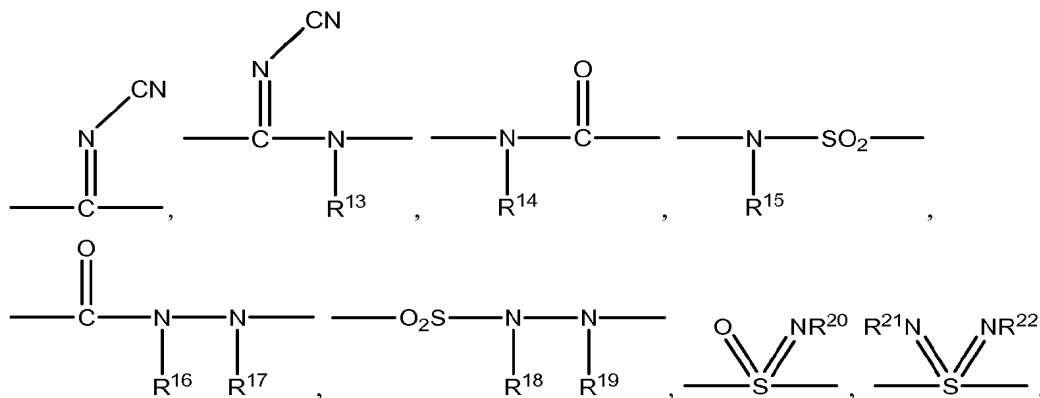
[00128] In another embodiment, the invention provides a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor compound of the formula:





(XXVII)

or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount, wherein m, n, r, s, and t are 0 or 1; p is 0, 1, or 2; V, W and X are selected from the group consisting of oxygen, hydrogen, R¹, R² or R³; Z and Y are selected from the group consisting of CHR⁹, SO₂, SO₃, CO, CO₂, O, NR¹⁰, SO₂ NR¹¹, CONR¹²,

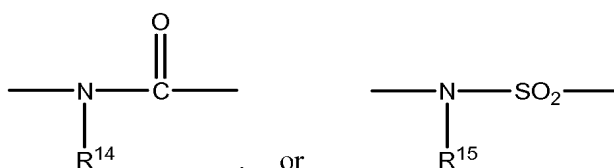


or Z may be absent; R⁶, R⁷, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²², R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, R²⁹, R³⁰, R³¹, R³², R³³, R³⁴, R³⁵, R³⁶, R³⁷, and R³⁸ are selected from the group consisting of hydrogen, lower alkyl, substituted alkyl, aryl, or substituted aryl; R⁴, R⁵ are selected from the group consisting of hydrogen, halo, nitro, cyano and U-R²³; U is selected from the group consisting of sulfur, oxygen, NR²⁴, CO, SO, SO₂, CO₂, NR²⁵ CO₂, NR²⁶ CONR²⁷, NR²⁸ SO₂, NR²⁹ SO₂ NR³⁰, SO₂ NR³¹, NR³² CO, CONR³³, PO₂ R³⁴ and PO₃ R³⁵ or U is absent; R¹, R², and R³ are selected from the group consisting of hydrogen, alkyl, alkoxy carbonyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, cyano, carboxy, carbamyl (*e.g.*, CONH₂) or substituted carbamyl further selected from CONH alkyl, CONH aryl, CONH aralkyl or cases where there are two substituents on the nitrogen selected

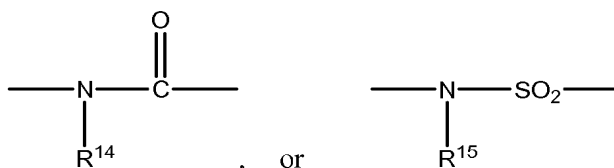
from alkyl, aryl or aralkyl; R^8 and R^{23} are selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo; any two of R^1 , R^2 , and R^3 can be joined to form a cycloalkyl group;

R, S and T are selected from the group consisting of CH_2 , CO and $CH(CH_2)_pQ$ wherein Q is NR^{36} , R^{37} , OR^{38} , or CN; and A, B, C and D are carbon, oxygen, sulfur or nitrogen with the provisos that:

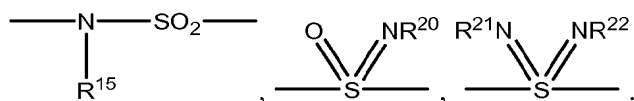
1. When m is zero then V and W are not both oxygen or,
2. W and X together can be oxygen only if Z is either absent, O, NR^{10} , CHR^9 ,



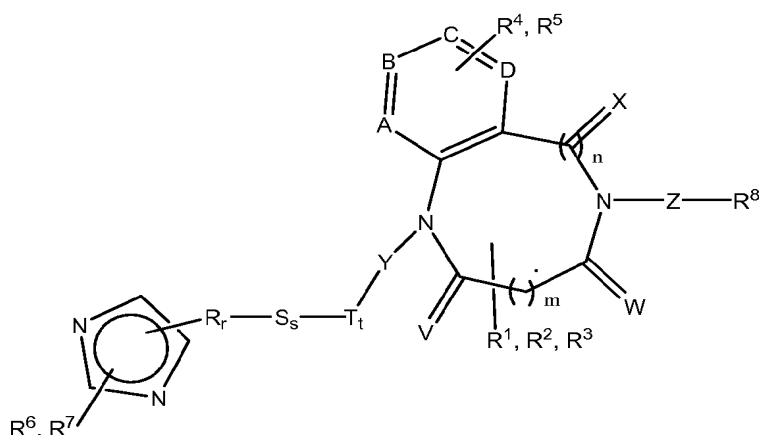
in formulas **XXIV** and **XXV**, and V and X together can be oxygen only if Y is O, NR^{10} , CHR^9 ,



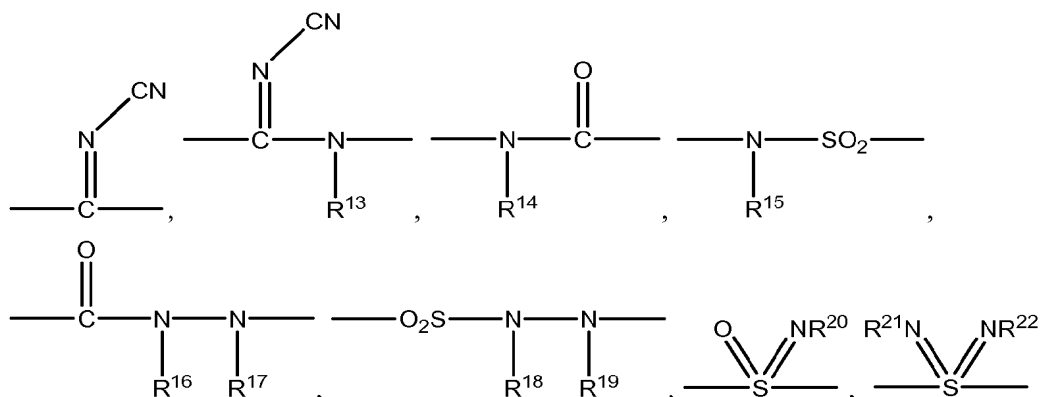
in formulas **XXVI** and **XXVII** or, 3. R^{23} may be hydrogen except when U is SO, SO_2 , NR^{25} , CO_2 or NR^{28} , SO_2 , or, 4. R^8 may be hydrogen except when Z is SO_2 , CO_2 , or



[00129] In one embodiment, the invention provides a method of treating a subject with a lysosomal storage disease, the method comprising, administering to the subject a farnesyl transferase inhibitor compound of the formula:

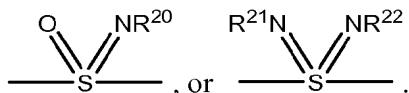


or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount, wherein n is 1; r, s and t are 0 or 1; p is 0, 1 or 2; V, W and X are selected from the group consisting of oxygen, hydrogen, R¹, R² and R³;



Z and Y are selected from the group consisting of CHR⁹, SO₂, SO₃, CO, CO₂, O, NR¹⁰, SO₂ NR¹¹, CONR¹², or Z may be absent; R⁶, R⁷, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²², R²⁴, R²⁵, R²⁶, R²⁸, R²⁹, R³⁰, R³¹, R³², R³³, R³⁴, R³⁵, R³⁶, R³⁷, and R³⁸ are selected from the group consisting of hydrogen, lower alkyl, substituted alkyl, aryl and substituted aryl; R⁴ and R⁵ are selected from the group consisting of hydrogen, halo, nitro, cyano and U--R²³; U is selected from the group consisting of sulfur, oxygen, NR²⁴, CO, SO, SO₂, CO₂, NR²⁵ CO₂, NR²⁶ CONR²⁷, NR²⁸ SO₂, NR²⁹ SO₂ NR³⁰, SO₂ NR³¹, NR³² CO, CONR³³, PO₂ R³⁴ and PO₃ R³⁵ or U is absent; R¹, R² and R³ are selected from the group consisting of hydrogen, alkyl, alkoxycarbonyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, cyano, carboxy, carbamyl and substituted carbamyl; R⁸ and R²³ are selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo and

substituted heterocyclo; any two of R^1 , R^2 and R^3 may be joined to form a cycloalkyl group; R, S and T are selected from the group consisting of CH_2 , CO and $CH(CH_2)_pQ$ wherein Q is NR^{36} , R^{37} , OR^{38} or CN; and A, B, C and D are carbon; with the provisos that V and W are not both oxygen; W and X together may be oxygen only if Z is either absent, O, NR^{10} , CHR^9 , $--N(R^{14})--C(O)--$, $--N(R^{15})--SO_2--$; R^{23} may be hydrogen except when U is SO , SO_2 , NR^{25} , CO_2 or NR^{28} , SO_2 ; and R^8 may be hydrogen except when Z is SO_2 , CO_2 , $--N(R^{15})--SO_2$,



[00130] In yet another embodiment of the invention, the compound is selected from the group consisting of:

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

8-Chloro-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-4-(1H-imidazol-4-yl-methyl)-1-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-yl-methyl)-2-methyl-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-4-(1-naphthalenylcarbonyl)-1-[[1-(phenylmethyl)-1H-imidazol-5-yl]methyl]-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-(1H-imidazol-4-yl-methyl)-4-(1-naphthalenylsulfonyl)-1H-1,4-benzodiazepine, hydrochloride;

(S)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-[2-(methylthio)ethyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-yl-methyl)-N-methyl-N-phenyl-4H-1,4-benzodiazepine-4-carboxamide, hydrochloride;

2-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-yl-methyl)-1H-1,4-benzodiazepin-4-yl]sulfonyl]benzoic acid, methyl ester, hydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-2-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-[3-(1H-imidazol-2-yl)propyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

1-[3-Amino-3-(1H-imidazol-2-yl)propyl]-2,3,4,5-tetrahydro-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-methyl-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

(S)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-[2-(methylthio)ethyl]-4-(1-naphthalenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-9-methyl-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-4-(1H-imidazol-4-ylmethyl)-9-methyl-1-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

1-[[2-(2-Aminoethyl)-1H-imidazol-4-yl]methyl]-2,3,4,5-tetrahydro-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

1-[[2-Aminomethyl)-1H-imidazol-4-yl]methyl]-2,3,4,5-tetrahydro-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]acetamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-8-nitro-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-8-amino-1H-1,4-benzodiazepine, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]benzamide, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]cyclohexanamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-[2-(1H-imidazol-4-yl)ethyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-[2-(1H-imidazol-4-yl)ethyl]-4-(1-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-[2-(1H-imidazol-4-yl)ethyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

1-[[1-(2-Aminoethyl)-1H-imidazol-5-yl]methyl]-2,3,4,5-tetrahydro-4-(1-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine-4-carboxylic acid, phenylmethyl ester;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[2-(trifluoromethoxy)benzoyl]-1H-1,4-benzodiazepine;

1,2,3,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-N-methyl-N,7-diphenyl-4H-1,4-benzodiazepine-4-carboxamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-(1-piperidinylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-pyridin-2-yl-1H-1,4-benzodiazepine, trihydrochloride;

7-(2-Furanyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-(2-thienyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-[3-(1H-imidazol-2-yl)propyl]-4-(1-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-2,3,4,5-tetrahydro-4-(1H-imidazol-4-ylmethyl)-1-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

8-Chloro-2,3,4,5-tetrahydro-4-(1H-imidazol-4-ylmethyl)-1-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-4-(1H-imidazol-4-ylmethyl)-1-(1-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, hydrochloride; 2,3,4,5-Tetrahydro-1,4-bis(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trifluoroacetate;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-methoxy-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine-7-carboxylic acid, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-5-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-cyclohexyl-1H-1,4-benzodiazepine, 2.5 hydrochloride;

7-Butyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

1-[[2-(2-Aminoethyl)-1H-imidazol-4-yl]methyl]-2,3,4,5-tetrahydro-4-(1-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

1-[[2-(Aminomethyl)-1H-imidazol-4-yl]methyl]-2,3,4,5-tetrahydro-4-(1-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-8-[N,N-bis(phenyl-methyl)amino]-1H-1,4-benzodiazepine, trihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-yl-methyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]phenylsulfonamide, dihydrochloride;

N-Phenyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-yl-methyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine-7-carboxamide, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-3-methylbenzamide, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-4-methylbenzamide, dihydrochloride;

3-Chloro-N-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-yl-methyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]benzamide, dihydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-[[2-[(dimethylamino)-methyl]-1H-imidazol-4-yl]methyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-(4-Chlorophenyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-(3-Aminophenyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

1-Methyl-N-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-1H-pyrrole-2-carboxamide, trihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-3-furancarboxamide, dihydrochloride;

7-(3-Chlorophenyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2-Methyl-N-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]benzamide, dihydrochloride;

N-Phenyl-N'-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]urea, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-(3-pyridinyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-9-methoxy-4-(1-naphthalenylcarbonyl)-1H-1,4-diazepine, dihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-[2-(methylthio)ethyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-3-(2-hydroxyethyl)-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trifluoroacetate;

2,3,4,5-Tetrahydro-4-(1H-imidazol-4-ylmethyl)-3-[2-(methylthio)ethyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(S)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

4-Acetyl-7-bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-4-(1H-imidazol-4-ylmethyl)-1-(1-naphthalenylcarbonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, 1.5 hydrochloride;

7-Bromo-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-carboxamide, trifluoroacetate;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

4-Acetyl-7-bromo-3-[(4-chlorophenyl)methyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

N-Cyclohexyl-N'-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]urea, dihydrochloride;

2,2-Dimethyl-N-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]propanamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylsulfonyl)-7-phenyl-1H-1,4-benzodiazepine, monohydrochloride;

- 4-Acetyl-7-bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(2-naphthalenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;
- 4-Acetyl-7-bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(1-naphthalenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;
- 7-(2-Chlorophenyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, monohydrochloride;
- 1-Methyl-N-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-2-piperidinecarboxamide, trihydrochloride;
- N-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-4-morpholinecarboxamide, dihydrochloride;
- N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-3-methylbutanamide, dihydrochloride;
- 1,2,3,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,N,7-triphenyl-4H-1,4,2,5-benzodiazepine-4-carboxamide, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[(4-phenyl-1,2,3-thiadiazol-5-yl)carbonyl]-1H-1,4-benzodiazepine, trifluoroacetate;
- 8-[[[(Cyclohexylamino)carbonyl]amino]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-4-carboxylic acid, 1,1-dimethylethyl ester;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-8-[[[(4-methylphenyl)sulfonyl]amino]-3-(phenylmethyl)-1H-1,4-benzodiazepine-4-carboxylic acid, 1,1-dimethylethylester;
- 7-Bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-5H-1,4-benzodiazepin-5-one, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[1-oxo-3-(1-piperidinyl)propyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(4-quinolinylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;
- 4-[(5-Bromo-3-pyridinyl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- (S)-4-[2-(Dimethylamino)-1-oxo-3-phenylpropyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-4-[4-hydroxy-3-(4-morpholinyl-methyl)benzoyl]-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

(S)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(1-methyl-2-pyrrolidinyl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[[2-(propylthio)-3-pyridinyl]carbonyl]-1H-1,4-benzodiazepine, trihydrochloride;

4-[(2-Chloro-6-methyl-4-pyridinyl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[[2-(phenylthio)-3-pyridinyl]carbonyl]-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[[2-(4-methylphenoxy)-3-pyridinyl]carbonyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-methoxy-3-pyridinyl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[(5-phenyl-4-oxazolyl)carbonyl]-1H-1,4-benzodiazepine, dihydrochloride;

4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[(tetrahydro-3-furanyl)carbonyl]-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-methoxyethoxy)acetyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[4-(4-morpholinylmethyl)benzoyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[4-(methylsulfonyl)benzoyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[1-oxo-3-(phenylsulfonyl)propyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(3-pyridinylacetyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(2-quinoxalinylnylcarbonyl)-1H-1,4-benzodiazepine, tetrahydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(4-isoquinolinylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

4-[(2-Chloro-3-pyridinyl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(3-pyridinylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

4-[(2,6-Dimethoxy-3-pyridinyl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(2-pyrazinylcarbonyl)-1H-1,4-benzodiazepine, tetrahydrochloride;

4-(2-Ethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-[3-(Dimethylamino)benzoyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[(1-phenylcyclopropyl)carbonyl]-1H-1,4-benzodiazepine, dihydrochloride;

4-[(Bicyclo[4.2.0]octa-1,3,5-trien-7-yl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-Benzoyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(2-Chlorobenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(2,3-Dichlorobenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

N-[2-[[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepin-4-yl]carbonyl]phenyl]-acetamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-phenoxybenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-methoxybenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(2,3-Dimethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(2,4-Dimethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(2,5-Dimethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(2,6-Dimethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(2,3-Dihydroxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-([1,1'-Biphenyl]-2-ylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-methylbenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(2,3-Dimethylbenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(3-Cyanobenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(3-Chlorobenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-phenoxybenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-methoxybenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(3,4-Dimethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(3,5-Dimethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-methylbenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(1,2-Dioxo-2-phenylethyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-[(2-Ethoxy-1-naphthalenyl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(Fluorophenylacetyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(Diphenylacetyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-4-(2-hydroxy-1-oxo-2-phenylpropyl)-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1H-indol-2-ylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1H-indol-3-ylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1H-indol-5-ylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(1-methyl-1H-indol-2-yl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(2-Benzofuranylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(3-pyridinylcarbonyl)-1H-1,4-benzodiazepine, N-oxide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(2-pyridinylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(2-quinolinylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(1-isoquinolinylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

4-(3-Chloro-2-nitrobenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-nitrobenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-methoxy-2-nitrobenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1H-indol-4-ylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-[(2,6-Dihydroxy-3-naphthalenyl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(1H-Benzimidazol-5-ylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

4-(1H-Benzotriazol-5-ylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(4-methoxy-2-quinolinyl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

N-[3-[[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepin-4-yl]carbonyl]phenyl]-acetamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-methyl-1-oxo-2-phenylpropyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-[2-(Dimethylamino)benzoyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

4-(3-Ethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-4-(2-hydroxy[1,1'-biphenyl]-3-ylcarbonyl)-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-4-[2-[(2-hydroxyethyl)thio]benzoyl]-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-methoxy-1-naphthalenyl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-4-[(2-hydroxy-4-quinolinyl)-carbonyl]-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2-[[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepin-4-yl]carbonyl]benzamide, dihydrochloride;

N-(1,1-Dimethylethyl)-2-[[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepin-4-yl]carbonyl]benzamide, dihydrochloride;

N-(4-Fluorophenyl)-N'-[3-[[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepin-4-yl]carbonyl]phenyl]urea, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(3-methyl-4-oxo-2-phenyl-4H-benzopyran-8-yl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[3-(trifluoromethoxy)benzoyl]-1H-1,4-benzodiazepine, dihydrochloride;

4-(2-Cyanobenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-[(4-methylphenyl)sulfonyl]amino]benzoyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(6-quinolinylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(8-quinolinylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

- 4-(Benzo[b]thiophen-2-ylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 4-[[4-(Dimethylamino)-1-naphthalenyl]carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(1H-purin-6-ylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methoxyphenylacetyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(5-methyl-1-phenyl-1H-pyrazol-4-yl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-(2-methylphenyl)-1-oxopropyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[(tetrahydro-4-phenyl-2H-pyran-4-yl)carbonyl]-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-(methylphenylamino)benzoyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(4-quinolinylcarbonyl)-1H-1,4-benzodiazepine, N-oxide, dihydrochloride;
- N-Methyl-N-(2-pyridinylmethyl)-2-[[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepin-4-yl]carbonyl]benzamide, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-isoquinolinylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-naphthalenylthio)acetyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:2);
- 4-[3-(3,4-Dimethoxyphenyl)-1-oxopropyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);
- 4-([1,1'-Biphenyl]-4-ylacetyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-naphthalenylacetyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);
- 4-([1,1'-Biphenyl]-2-ylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-phenyl-4-quinolinyl)carbonyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:3);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-pyridinylacetyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:3);

4-(9H-Fluoren-9-ylacetyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

(S)-4-[2-(Dimethylamino)-1-oxo-3-phenylpropyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:3);

(S)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-oxo-4-phenyl-3-oxazolidinyl)acetyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

4-(9-Acridinylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:3);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-phenoxybenzoyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[[4'-(trifluoromethyl)[1,1'-biphenyl]-2-yl]carbonyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(4-phenoxybenzoyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-oxo-4-phenylbutyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-phenoxyphenyl)acetyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-[(4-methylphenyl)sulfinyl]benzoyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-[(phenylmethyl)amino]benzoyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:3);

1,2,3,5-Tetrahydro-1-(1H-imidazol-4-yl-methyl)-N,N-diphenyl-4H-1,4-benzodiazepine-4-carboxamide, hydrochloride;

1,2,3,5-Tetrahydro-1-(1H-imidazol-4-yl-methyl)-a,7-diphenyl-4H-1,4-benzodiazepine-4-acetic acid, methyl ester, hydrochloride;

4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

- (R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, monohydrochloride;
- (R)-4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- 7-Bromo-4-[[2-(dimethylamino)ethyl]sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine, trifluoroacetate (1:2);
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[(1,2,3,4-tetrahydro-1-quinoliny)carbonyl]-1H-1,4-benzodiazepine, monohydrochloride;
- N-Ethyl-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,7-diphenyl-4H-1,4-benzodiazepine-4-carboxamide, monohydrochloride;
- 4-[(2,3-Dihydro-1H-indol-1-yl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, monohydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, trihydrochloride;
- (R)-4-[[2-(Dimethylamino)ethyl]sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:1);
- [2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]carbamic acid, cyclohexyl ester, dihydrochloride;
- (R)-7-Bromo-2,3,4,5-tetrahydro-1-(1-methyl-1H-imidazol-5-yl)methyl-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- 4-[2-(4-Chlorophenyl)-1,2-dioxoethyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, hydrochloride;
- 4-(1,2-Dioxopropyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, hydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-(4-nitrophenyl)-1,2-dioxoethyl]-7-phenyl-1H-1,4-benzodiazepine, hydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-(4-methoxyphenyl)-1,2-dioxoethyl]-7-phenyl-1H-1,4-benzodiazepine, hydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(3,3,3-trifluoro-1,2-dioxopropyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);
- (R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylacetyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(2-1H-imidazol-4-ylethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

8-[(Cyclohexylcarbonyl)amino]-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-carboxylic acid, methyl ester, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-1-piperidinecarboxamide, dihydrochloride;

(R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-carboxylic acid, ethyl ester, hydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-8-yl]cyclohexanecarboxamide, dihydrochloride;

(R)-7-Cyano-4-[[2-(dimethylamino)ethyl]sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[[2-(4-morpholinyl)ethyl]sulfonyl]-3-(phenylmethyl)-4H-1,4-benzodiazepine, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-methoxy-3-methylbenzoyl)-1H-1,4-benzodiazepin-8-yl]cyclohexanecarboxamide, dihydrochloride,

8-[(Cyclohexylcarbonyl)amino]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N-phenyl-1H-1,4-benzodiazepine-4-carboxamide, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-methylphenyl)sulfonyl]-1H-1,4-benzodiazepin-8-yl]cyclohexanamide, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-methoxyphenyl)carbonyl]-1H-1,4-benzodiazepin-8-yl]cyclohexanamide, dihydrochloride;

(R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-sulfonic acid, ethyl ester, hydrochloride;

(3R)-7-Bromo-1-[cyano(1H-imidazol-4-yl)methyl]-2,3,4,5-tetrahydro-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(3R)-1-[2-Amino-1-(1H-imidazol-4-yl)ethyl]-2,3,4,5-tetrahydro-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(3R)-1-[2-(Dimethylamino)-1-(1H-imidazol-4-yl)ethyl]-2,3,4,5-tetrahydro-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(3R)-1-[2-Amino-1-(1H-imidazol-4-yl)ethyl]-7-bromo-2,3,4,5-tetrahydro-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(3R)-1-[2-(Dimethylamino)-1-(1H-imidazol-4-yl)ethyl]-7-bromo-2,3,4,5-tetrahydro-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Cyano-1,3,4,5-tetrahydro-1-(1-methyl-1H-imidazol-5-ylmethyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-2H-1,4-benzodiazepin-2-one, monohydrochloride;

7-Cyano-1,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-2H-1,4-benzodiazepin-2-one, monohydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(2-phenylethyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-3-[(3-chlorophenyl)methyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Bromo-3-(cyclohexylmethyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-3-[(2-chlorophenyl)methyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

(S)-7-Bromo-3-(cyclohexylmethyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-[(4-methoxyphenyl)methyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

4-Acetyl-7-bromo-3-[(2-chlorophenyl)methyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

4-Acetyl-7-bromo-3-[(3-chlorophenyl)methyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-[(4-hydroxyphenyl)methyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-7-phenyl-3-(3-pyridinylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-8-(hydroxymethyl)-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-8-(phoxymethyl)-1H-1,4-benzodiazepine, dihydrochloride;

N-Cyclohexyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine-8-carboxamide, dihydrochloride;

N-(Cyclohexylmethyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine-8-carboxamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-N-(phenylmethyl)-1H-1,4-benzodiazepine-8-carboxamide, dihydrochloride;

(R)-4-Acetyl-7-[2-[(dimethylamino)methyl]phenyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-4-Acetyl-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-oxobutyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-methyl-1-oxopropyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-pyridinylacetyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(1-methylethyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[(trifluoromethyl)sulfonyl]-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-4-[(4-fluorophenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-4-[(3-cyanophenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(1-methyl-1H-imidazol-2-yl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-4-[(3-Bromophenyl)sulfonyl]-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-N-[5-[[7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-4-yl]sulfonyl]-4-methyl-2-thiazolyl]acetamide, dihydrochloride;

4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-phenyl-1,2-dioxoethyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-(4-pyridinyl)-4-[2-(trifluoromethoxy)benzoyl]-1H-1,4-benzodiazepine, trihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-4-(methylsulfonyl)-7-phenyl-3-(phenylmethyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(phenylacetyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

4-(2-Benzothiazolyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-7-(3-pyridinyl)-4-(trifluoroacetyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-7-(3-pyridinyl)-1H-1,4-benzodiazepine, trihydrochloride;

7-Bromo-3-[(1,1-dimethylethoxy)methyl]-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-5H-1,4-benzodiazepin-5-one;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phoxymethyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-2,3,4,5-tetrahydro-3-(hydroxymethyl)-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;

7-Bromo-3-[(1,1-dimethylethoxy)methyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

[7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-8-yl]carbamic acid, 2-methylpropyl ester, trihydrochloride;

[4-Acetyl-7-bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-8-yl]carbamic acid, 2-methylpropyl ester;

N-[4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-8-yl]cyclohexanecarboxamide, dihydrochloride;

[7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-8-yl]carbamic acid, 2-methylpropyl ester;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(phenylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, monohydrochloride;

7-Bromo-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-acetamide;

7-Bromo-4-[(dimethylamino)acetyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine;

(R)-7-Bromo-4-(1,2-dioxopropyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(R)-7-Bromo-4-(cyclopropylcarboonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1,4-bis(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,N-dimethyl-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-sulfonamide, monohydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, monohydrochloride;

(R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,N-dimethyl-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-carboxamide, monohydrochloride;

N,N-Diethyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carboxamide, monohydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(1-phenyl-1H-tetrazol-5-yl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-pyrazinylcarbonyl)-4H-1,4-benzodiazepine, monohydrochloride;

(R)-4-[7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepin-4-yl]-4-oxobutanoic acid, methyl ester, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(4-morpholinylcarbonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[[2-(1-pyrrolidinyl)ethyl]sulfonyl]-1H-1,4-benzodiazepine, dihydrochloride;

(S)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-7-phenyl-3-(3-pyridinylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(3-pyridinylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

- (R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(propylsulfonyl)-3-(3-pyridinylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(2-pyridinylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-7-(2-pyrimidinyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[(trifluoromethyl)sulfonyl]-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-4-(trifluoroacetyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-7-(4-pyridinyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(propylsulfonyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[(3,5-dimethyl-isoxazol-4-yl)sulfonyl]-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Cyano-4-[(4-cyanophenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[(2,2,2-trifluoroethyl)sulfonyl]-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-[(5-Bromo-2-thienyl)sulfonyl]-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(4-methoxyphenyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;
- N-[[7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepin-3-yl]methyl]benzamide, dihydrochloride;
- (R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,N-dimethyl-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-sulfonamide, hydrochloride;
- (R)-7-Cyano-1,2,3,5-tetrahydro-N,N-dimethyl-1-[(1-methyl-1H-imidazol-5-yl)methyl]-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-sulfonamide, hydrochloride;

(R)-7-Chloro-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Chloro-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Chloro-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-4-(phenylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(pyridin-3-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, tetrahydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-2-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, trihydrochloride;

(R)-7-Chloro-2,3,4,5-tetrahydro-1-(1-methyl-imidazol-5-ylmethyl)-4-[(2-morpholin-4-yl-ethyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Chloro-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-morpholin-4-yl-ethyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Chloro-4-[(dimethylamino)sulfonyl]-1-[(1-methyl-1H-imidazol-5-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Chloro-2,3,4,5-tetrahydro-1-(1-methyl-imidazol-5-ylmethyl)-4-[(4-methyl-piperidin-4-yl-ethyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1-methyl-imidazol-5-ylmethyl)-4-[(4-methyl-piperidin-4-yl-ethyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-carboxylic acid, isopropyl ester, hydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-4-[[2-(1H-imidazol-1-yl)ethyl]sulfonyl]-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(propylsulfonyl)-3-(3-pyridinylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-5-one, hydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-1-ylacetyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

1,2,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-2-(2-phenylethyl)-3H-1,4-benzodiazepin-3-one;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-2-(2-phenylethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-7-phenyl-3-(4-pyridinylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-2-ylmethyl)-4-(phenylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, hydrochloride;

(R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,N-dimethyl-3-(3-pyridinylmethyl)-4H-1,4-benzodiazepine-4-carboxamide, dihydrochloride;

(R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,N-dimethyl-3-(3-pyridinylmethyl)-4H-1,4-benzodiazepine-4-sulfonamide, dihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1-(4-cyanophenylmethyl)-imidazol-5-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, hydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1-(4-cyanophenylmethyl)-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, hydrochloride;

(R)-4-Benzoyl-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-3-(pyridin-3-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-3-(pyridin-3-ylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine, trihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-[(1H-imidazol-4-yl)methyl]-3-(pyridin-3-ylmethyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-7-phenyl-3-(phenylmethyl)-1H-1,4-benzodiazepine;

1,2,3,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-N-(1-naphthalenyl)-7-phenyl-4H-1,4-benzodiazepine-4-carboxamide, monohydrochloride;

(S)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2,3-dimethylbenzoyl)-1H-1,4-benzodiazepin-8-yl]cyclohexanecarboxamide, dihydrochloride;

(R)-7-Cyano-N-[2-(dimethylamino)ethyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N-methyl-3-(phenylmethyl)-1H-1,4-benzodiazepine-4-carboxamide, trifluoroacetate (1:2);

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-2-oxo-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(R)-7-Cyano-4-(2-furanylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:1);

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(4-nitrophenyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[[4-(4-methyl-1-piperazinyl)phenyl]sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[[4-(dimethylamino)phenyl]sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(R)-7-Bromo-4-[[2-(dimethylamino)ethyl]sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(3-pyridinylsulfonyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-4-yl)methyl]-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-4-[[3-(Dimethylamino)propyl]sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trihydrochloride;

4-Butyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[[2-(4-morpholinyl)ethyl]sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-4-[[2-(4-morpholinyl)ethyl]sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-1-(1H-imidazol-4-ylmethyl)-4-(4-morpholinylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-1-[(1-methyl-1H-imidazol-5-yl)methyl]-4-[(4-morpholinyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(4-aminophenyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(4-pyridylthio)acetyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

N-(4-Chlorophenyl)-N'-cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4H-1,4-benzodiazepine-4-imidamide, monohydrochloride;

4-Acetyl-7-bromo-1,2,4,5, 1',3'-hexahydro-1-(1H-imidazol-4-ylmethyl)spiro[3H-1,4-benzodiazepine-3,2'-[2H]indene], dihydrochloride;

7-Bromo-4-[3-(dimethylamino)-1-oxopropyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:1);

(R)-2,3,4,5-Tetrahydro-1-(1-methyl-1H-imidazol-5-ylmethyl)-4-(phenylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, monohydrochloride;

2,3,4,5-Tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)-methyl]-4-(methyl-sulfonyl)-7-phenyl-3-(pyridin-3-yl-methyl)-1H-1,4-benzodiazepine, hydrochloride (1:1.5), trifluoroacetate (1:0.75) salt;

4-[4-(Fluorophenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-2-(2-phenylethyl)-1H-1,4-benzodiazepine, monohydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-yl-methyl)-4-(methyl-sulfonyl)-2-(2-phenylethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1-methyl-1H-imidazol-5-ylmethyl)-4-[[2-(1-morpholinyl)ethyl]sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methyl-sulfonyl)-3-(4-bromophenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methyl-sulfonyl)-3-(thiazol-4-ylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(propyl-sulfonyl)-3-(thiazol-4-ylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(propylsulfonyl)-3-(4-bromophenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(pyridin-3-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, trihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-1-methyl-imidazol-5-ylmethyl)-3-(pyridin-3-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(phenyl-sulfonyl)-3-(4-cyanophenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

- (R)-7-Cyano-4-[(N-methyl-N-phenylmethyl)aminosulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Cyano-4-[N-(tetrahydroisoquinoliny)sulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(phenylsulfonyl)-3-(2-thienylmethyl)-1H-1,4-benzodiazepine, hydrochloride;
- cis-2,3,4,5-Tetrahydro-1,5-bis(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,5-benzodiazepine-2-carboxylic acid ethyl ester, trifluoroacetate (1:2);
- (R)-7-Cyano-4-[(N-piperidiny)sulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-1-methyl-imidazol-5-ylmethyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine, hydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(pyridin-3-ylmethyl)-4-[[2-(dimethylamino)ethyl]sulfonyl]-1H-1,4-benzodiazepine, trihydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-1-methyl-imidazol-5-ylmethyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine, hydrochloride;
- N-(Cyano)-N'-methyl-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4H-1,4-benzodiazepine-4-imidamide, hydrochloride;
- (R)-7-Cyano-4-[(2-nitrophenyl)-sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenyl-methyl)-1H-1,4-benzodiazepine, hydrochloride;
- R)-7-Cyano-4-[(4-methyl-phenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;
- (R)-7-Cyano-4-(butylsulfonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;
- (R)-7-Cyano-4-[(2-trifluoro-methylphenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;
- (R)-7-Cyano-4-[(2-trifluoromethoxyphenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;
- (R)-7-Cyano-4-[(2-methoxy-carbonylphenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;
- (R)-7-Cyano-4-[(2-methyl-sulfonylphenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(((4-methylsulfonyl)-phenyl)-sulfonyl)-1H-1,4-benzodiazepine;

- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(((4-trifluoromethyl)-phenyl)-sulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((3-methoxypropyl)-sulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((3,4-dimethoxyphenyl)-sulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-((4-fluorophenyl)methyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-4-[(N-cyclopropylmethyl-N-propyl)-aminosulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-4-[(N,N-(dibutylamino))-sulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine;
- 1,2,3,4-Tetrahydro-7-bromo-4-[(1H-imidazol-4-yl)methyl]-2-phenylmethyl-1-(methylsulfonyl)quinoxaline;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((imidazol-4-yl)methylsulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-((2-thienyl)methyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-((2-thienyl)methyl)-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((3-methylthiopropyl)-sulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(((3-methylthio)-propyl)-sulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(((3-methylsulfonyl)-propyl)-sulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((2-methylpropyl)-sulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-30 (cyclopentylsulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((4,4,4-trifluorobutyl)-sulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((phenylmethyl)-sulfonyl)-1H-1,4-benzodiazepine;

- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[[2-(5-(N-benzoyl)-aminomethyl)-thienyl]-sulfonyl]-1H-1,4-benzodiazepine
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[[2-(1-(3-chloro-5-methyl-pyridin-2-yl))-pyrrolyl]-sulfonyl]-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((4-carboxyphenyl)-sulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(((3-methyl-1,2,4-oxadiazol-5-yl)-phenyl)-sulfonyl]-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((2,5-dimethoxyphenyl)-sulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-4-[(N-tetrahydroquinolinyl)sulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-4-[(N,N-bis-[1-(2-methylpropyl)amino]-sulfonyl)-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-4-[(N-methyl-N-phenyl)aminosulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(2-(2,6-dimethylphenyl)-ethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1-(N-phthalimidoethyl)-imidazol-5-ylmethyl)-3-(phenylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-[(2-(N,N-dimethylamino)-ethyl)-imidazol-5-ylmethyl]-3-(phenylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-[(2-aminoethyl)-imidazol-5-ylmethyl]-3-(phenylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;
- (R)-4-(methanesulfonyl)-2,3,4,5-tetrahydro-1-[(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-8-oxo-pyrimidino[4,5-e]-1,4-diazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-((4-(2-methoxyethoxy)-phenyl)methyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-((4-(2-(dimethylamino)-ethoxy)-phenyl)methyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylsulfonyl)-3-(phenylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylsulfonyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylsulfonyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylsulfonyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-1-phenyl-ethyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-1-phenyl-ethyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-1-phenyl-ethyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-1-phenyl-ethyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-1-phenyl-ethyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-1-phenyl-ethyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-1-phenyl-ethyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-1-phenyl-ethyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-1-phenyl-ethyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-1-phenyl-ethyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-1-phenyl-ethyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-1-phenyl-ethyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-1-phenyl-ethyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-1-phenyl-ethyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-1-phenyl-ethyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-1-phenyl-ethyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-phenylcyclopropyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-phenylcyclopropyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-phenylcyclopropyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-phenylcyclopropyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-phenylcyclopropyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-phenylcyclopropyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-phenylcyclopropyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-phenylcyclopropyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-phenylcyclopropyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-phenylcyclopropyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-phenylcyclopropyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-phenylcyclopropyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-phenylcyclopropyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-phenylcyclopropyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-phenylcyclopropyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-phenylcyclopropyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[(2-(5-(pyridin-2-yl))-thienyl)-sulfonyl]-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[(2-(5-(1,2-isoxazol-3-yl))-thienyl)-sulfonyl]-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(3-(1H-imidazol-2-yl)-propyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(3-(1H-imidazol-2-yl)-propyl)-3-(phenylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(3-(1H-imidazol-2-yl)-propyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(3-(1H-imidazol-2-yl)-propyl)-3-(phenylmethyl)-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(2-(1H-imidazol-2-yl)-ethylsulfonyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(2-(1H-imidazol-2-yl)-ethylsulfonyl)-3-(phenylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(2-(1H-imidazol-2-yl)-ethylsulfonyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

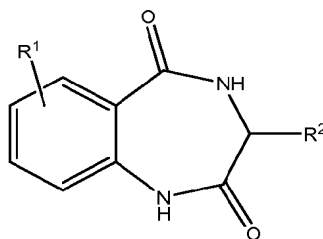
(R)-7-Cyano-2,3,4,5-tetrahydro-1-(2-(1H-imidazol-2-yl)-ethylsulfonyl)-3-(phenylmethyl)-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((1-oxoethyl)-amino)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(methanesulfonylamino)-1H-1,4-benzodiazepine; and

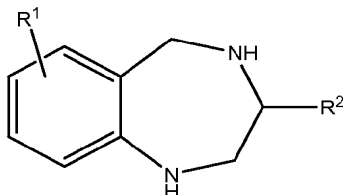
(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(phenylsulfonylamino)-1H-1,4-benzodiazepine.

[00131] In another embodiment of the invention, the compound has the formula:



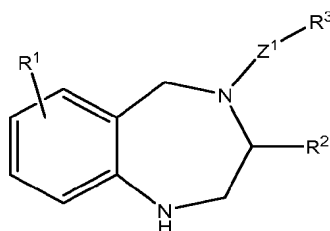
wherein R_1 is selected from Cl, Br, phenyl, pyridyl, and cyano; and R_2 is selected from substituted aralkyl and substituted heterocycloalkyl.

[00132] In yet another embodiment of the invention the compound has the formula:



wherein R_1 is selected from Cl, Br, phenyl, pyridyl, and cyano; and R_2 is selected from substituted aralkyl and substituted heterocycloalkyl.

[00133] In another embodiment of the invention, the compound has the formula:



wherein

R_1 is Cl, Br, phenyl, pyridyl or cyano;

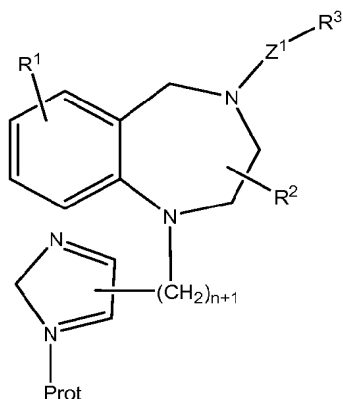
R_2 is substituted aralkyl or substituted heterocycloalkyl;

R_3 is substituted alkyl, substituted aryl or substituted heterocyclo;

Z_1 is CO, SO₂, CO₂, CONHR₅, SO₃, SO₂ NR₅, or C(NCN)NR₅; and

R_5 is hydrogen, lower alkyl, substituted alkyl, aryl or substituted aryl.

[00134] In one aspect of the invention, the compound has the formula:



wherein

R_1 is selected from Cl, Br, phenyl, pyridyl or cyano;

R_2 is selected from substituted aralkyl or substituted heterocycloalkyl;

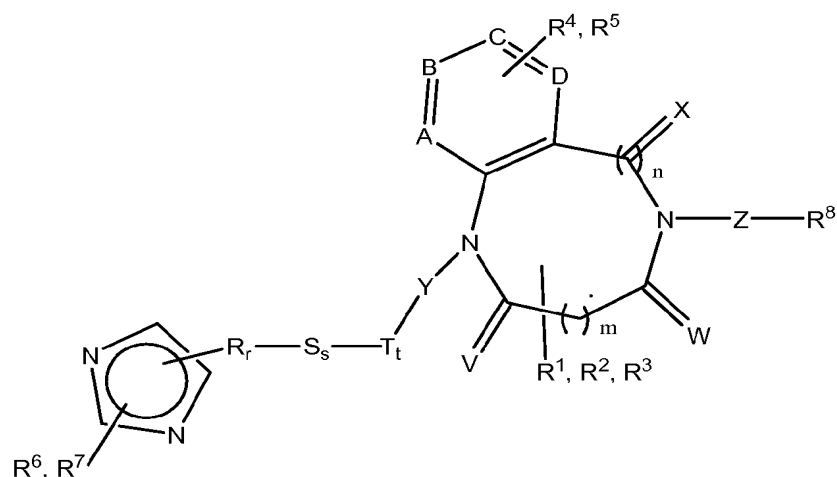
R_3 is selected from substituted alkyl, substituted aryl or substituted heterocyclo;

Z_1 is selected from CO, SO₂, CO₂, CONHR₅, SO₃, SO₂ NR₅, or C(NCN)NR₅;

Prot is triphenylmethyl or Boc; and

R_5 is selected from hydrogen, lower alkyl, substituted alkyl, aryl or substituted aryl.

[00135] In one aspect, the invention provides a method of treating a subject with a lysosomal storage disease, the method comprising administering to the subject a farnesyl transferase inhibitor compound of the formula:



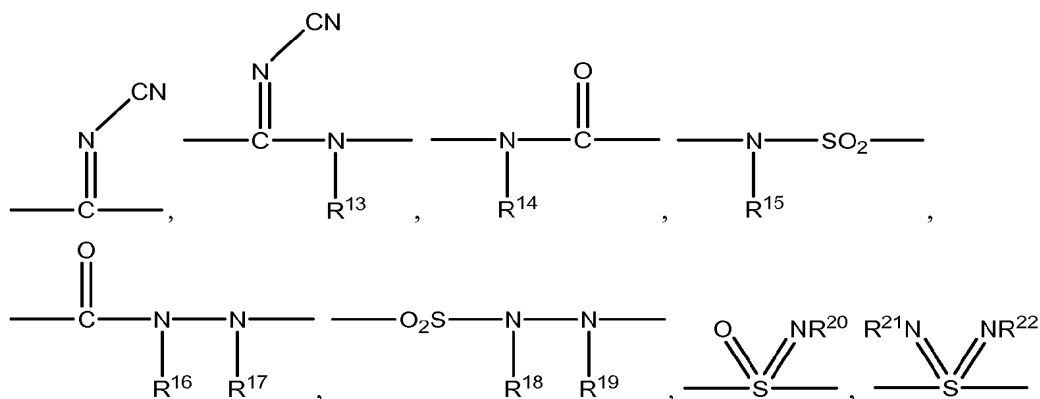
or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount, wherein

n is 1;

r , s and t are 0 or 1;

p is 0, 1 or 2;

V , W and X are selected from the group consisting of oxygen, hydrogen, R^1 , R^2 and R^3 ;



Z and Y are selected from the group consisting of CHR^9 , SO_2 , SO_3 , CO , CO_2 , O , NR^{10} , $\text{SO}_2 \text{NR}^{11}$, CONR^{12} ,

or Z may be absent;

R^6 , R^7 , R^9 , R^{10} , R^{11} , R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} , R^{19} , R^{20} , R^{21} , R^{22} , R^{24} , R^{25} , R^{26} , R^{28} , R^{29} , R^{30} , R^{31} , R^{32} , R^{33} , R^{34} , R^{35} , R^{36} , R^{37} , and R^{38} are selected from the group consisting of hydrogen, lower alkyl, substituted alkyl, aryl and substituted aryl;

R^4 and R^5 are selected from the group consisting of hydrogen, halo, nitro, cyano and U--R^{23} ;

U is selected from the group consisting of sulfur, oxygen, NR^{24} , CO , SO , SO_2 , CO_2 , NR^{25} , CO_2 , NR^{26} , CONR^{27} , NR^{28} , SO_2 , NR^{29} , $\text{SO}_2 \text{NR}^{30}$, $\text{SO}_2 \text{NR}^{31}$, NR^{32} , CO , CONR^{33} , $\text{PO}_2 \text{R}^{34}$ and $\text{PO}_3 \text{R}^{35}$ or U is absent;

R^1 , R^2 and R^3 are selected from the group consisting of hydrogen, alkyl, alkoxycarbonyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, cyano, carboxy, carbamyl and substituted carbamyl;

R^8 and R^{23} are selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo and substituted heterocyclo;

any two of R^1 , R^2 and R^3 may be joined to form a cycloalkyl group;

R, S and T are selected from the group consisting of CH_2 , CO and $\text{CH}(\text{CH}_2)_p\text{Q}$ wherein Q is NR^{36} , R^{37} , OR^{38} or CN ; and

A, B, C and D are carbon;

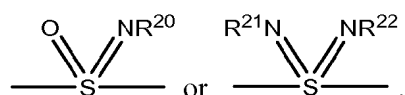
with the provisos that

V and W are not both oxygen;

W and X together may be oxygen only if Z is either absent, O , NR^{10} , CHR^9 , $\text{--N(R}^{14})\text{--C(O)--}$, $\text{--N(R}^{15})\text{--SO}_2\text{--}$;

R^{23} may be hydrogen except when U is SO , SO_2 , $\text{NR}^{25} \text{CO}_2$ or $\text{NR}^{28} \text{SO}_2$; and

R^8 may be hydrogen except when Z is SO_2 , CO_2 , $\text{--N(R}^{15})\text{--SO}_2$,



[00136] In one embodiment of the invention the pharmaceutically acceptable salt is mesylate. In one embodiment of the invention the compound is (R)-7-cyano-2,3,4,5-

tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine, mesylate salt. In yet another embodiment of the invention the compound is selected from the group consisting of:

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

8-Chloro-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-yl-methyl)-2-methyl-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-4-(1-naphthalenylcarbonyl)-1-[[1-(phenylmethyl)-1H-imidazol-5-yl]methyl]-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-(1H-imidazol-4-yl-methyl)-4-(1-naphthalenylsulfonyl)-1H-1,4-benzodiazepine, hydrochloride;

(S)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-[2-(methylthio)ethyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-yl-methyl)-N-methyl-N-phenyl-4H-1,4-benzodiazepine-4-carboxamide, hydrochloride;

2-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-yl-methyl)-1H-1,4-benzodiazepin-4-yl]sulfonyl]benzoic acid, methyl ester, hydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-2-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-[3-(1H-imidazol-2-yl)propyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

1-[3-Amino-3-(1H-imidazol-2-yl)propyl]-2,3,4,5-tetrahydro-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-methyl-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

(S)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-[2-(methylthio)ethyl]-4-(1-naphthalenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-9-methyl-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

1-[[2-(2-Aminoethyl)-1H-imidazol-4-ylmethyl]-2,3,4,5-tetrahydro-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

1-[[2-Aminomethyl)-1H-imidazol-4-yl]methyl]-2,3,4,5-tetrahydro-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]acetamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-naphtho[2,3-e]-1,4-diazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-8-nitro-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-8-amino-1H-1,4-benzodiazepine, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]benzamide, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]cyclohexanamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-[2-(1H-imidazol-4-yl)ethyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-[2-(1H-imidazol-4-yl)ethyl]-4-(1-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-[2-(1H-imidazol-4-yl)ethyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

1-[[1-(2-Aminoethyl)-1H-imidazol-5-yl]methyl]-2,3,4,5-tetrahydro-4-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine-4-carboxylic acid, phenylmethyl ester;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[2-(trifluoromethoxy)benzoyl]-1H-1,4-benzodiazepine;

1,2,3,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-N-methyl-N,7-diphenyl-4H-1,4-benzodiazepine-4-carboxamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-(1-piperidinylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-pyridin-2-yl-1H-1,4-benzodiazepine, trihydrochloride;

7-(2-Furanyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-(2-thienyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-[3-(1H-imidazol-2-yl)propyl]-4-(1-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1,4-bis(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trifluoroacetate;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-methoxy-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine-7-carboxylic acid, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-5-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-cyclohexyl-1H-1,4-benzodiazepine, 2,5 hydrochloride;

7-Butyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

1-[[2-(2-Aminoethyl)-1H-imidazol-4-yl]methyl]-2,3,4,5-tetrahydro-4-(1-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

1-[[2-(Aminomethyl)-1H-imidazol-4-yl]methyl]-2,3,4,5-tetrahydro-4-(1-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-8-[N,N-bis(phenyl-methyl)amino]-1H-1,4-benzodiazepine, trihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-yl-methyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8yl]phenylsulfonamide, dihydrochloride;

N-Phenyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-yl-methyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine-7carboxamide, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-3-methylbenzamide, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-4-methylbenzamide, dihydrochloride;

3-Chloro-N-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-yl-methyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzo-diazepin-8-yl]benzamide, dihydrochloride;

7-Bromo-2,3,4,5,-tetrahydro-1-[[2-[(dimethylamino)-methyl]-1H-imidazol-4-yl]methyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-(4-Chlorophenyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-(3-Aminophenyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

1-Methyl-N-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-1H-pyrrole-2-carboxamide, trihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-3-furancarboxamide, dihydrochloride;

7-(3-Chlorophenyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2-Methyl-N-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]benzamide, dihydrochloride;

N-Phenyl-N'-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]urea, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-7-(3-pyridinyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-9-methoxy-4-(1-naphthalenylcarbonyl)-1H-1,4-diazepine, dihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-[2-(methylthio)ethyl]-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-3-(2-hydroxyethyl)-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(S)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

4-Acetyl-7-bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

7-Bromo-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-carboxamide, trifluoroacetate;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

4-Acetyl-7-bromo-3-[(4-chlorophenyl)methyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-naphtho[2,3-e]-1,4-diazepine, monohydrochloride;

N-Cyclohexyl-N'-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]urea, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-naphtho[2,3-e]-1,4-diazepine, monohydrochloride;

2,2-Dimethyl-N-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]propanamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylsulfonyl)-7-phenyl-1H-1,4-benzodiazepine, monohydrochloride;

4-Acetyl-7-bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(2-naphthalenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

4-Acetyl-7-bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(1-naphthalenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-(2-Chlorophenyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, monohydrochloride;

1-Methyl-N-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-2-piperidinecarboxamide, trihydrochloride;

N-[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-4-morpholinecarboxamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-3-methylbutanamide, dihydrochloride;

1,2,3,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,N,7-triphenyl-4H-1,4-benzodiazepin -carboxamide, dihydrochloride;

1,2,3,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-naphtho[2,3-e]-1,4-diazepine-4-carboxylic acid, methyl ester, monohydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[(4-phenyl-1,2,3-thiadiazol-5-yl)carbonyl]-1H-1,4-benzodiazepine, trifluoroacetate;

8-[[[(Cyclohexylamino)carbonyl]amino]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-4-carboxylic acid, 1,1-dimethylethyl ester;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-8-[[[(4-methylphenyl)sulfonyl]amino]-3-(phenylmethyl)-1H-1,4-benzodiazepine-4-carboxylic acid, 1,1-dimethylethylester;

7-Bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-5H-1,4-benzodiazepin-5-one, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[1-oxo-3-(1-piperidiny)propyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(4-quinoliny)carbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

4-[(5-Bromo-3-pyridiny)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

(S)-4-[2-(Dimethylamino)-1-oxo-3-phenylpropyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-4-[4-hydroxy-3-(4-morpholiny)methyl]benzoyl]-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

(S)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(1-methyl-2-pyrrolidiny)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[[2-(propylthio)-3-pyridiny]carbonyl]-1H-1,4-benzodiazepine, trihydrochloride;

4-[(2-Chloro-6-methyl-4-pyridiny)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[[2-(phenylthio)-3-pyridiny]carbonyl]-1H-1,4-benzodiazepine, trihydrochloride;

- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[[2-(4-methylphenoxy)-3-piperidinyl]carbonyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-methoxy-3-pyridinyl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[(5-phenyl-4-oxazolyl)carbonyl]-1H-1,4-benzodiazepine, dihydrochloride;
- 4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[(tetrahydro-3-furanyl)carbonyl]-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-methoxyethoxy)acetyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(4-(4-morpholinylmethyl)benzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(4-(4-morpholinylmethyl)benzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[4-(methylsulfonyl)benzoyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[1-oxo-3-(phenylsulfonyl)propyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(3-pyridinylacetyl)-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(2-quinoxalinylylcarbonyl)-1H-1,4-benzodiazepine, tetrahydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(4-isoquinolinylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- 4-[(2-Chloro-3-pyridinyl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(3-pyridinylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;
- 4-[(2,6-Dimethoxy-3-pyridinyl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(2-pyrazinylcarbonyl)-1H-1,4-benzodiazepine, tetrahydrochloride;

- 4-(2-Ethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 4-[3-(Dimethylamino)benzoyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[(1-phenylcyclopropyl)carbonyl]-1H-1,4-benzodiazepine, dihydrochloride;
- 4-[(Bicyclo[4.2.0]octa-1,3,5-trien-7-yl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 4-Benzoyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 4-(2-Chlorobenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 4-(2,3-Dichlorobenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- N-[2-[[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepin-4-yl]carbonyl]phenyl]acetamide, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-phenoxybenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-methoxybenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 4-(2,3-Dimethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 4-(2,4-Dimethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 4-(2,5-Dimethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 4-(2,6-Dimethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 4-(2,3-Dihydroxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 4-([1,1'-Biphenyl]-2-ylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-methylbenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(2,3-Dimethylbenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(3-Cyanobenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(3-Chlorobenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-phenoxybenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-methoxybenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(3,4-Dimethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(3,5-Dimethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-methylbenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(1,2-Dioxo-2-phenylethyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-[(2-Ethoxy-1-naphthalenyl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-naphthalenylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(Fluorophenylacetyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(Diphenylacetyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-4-(2-hydroxy-1-oxo-2-phenylpropyl)-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1H-indol-2-ylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1H-indol-3-ylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1H-indol-5-ylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(1-methyl-1H-indol-2-yl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(2-Benzofuranylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(3-pyridinylcarbonyl)-1H-1,4-benzodiazepine, N-oxide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(2-pyridinylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(2-quinolinylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(1-isoquinolinylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

4-(3-Chloro-2-nitrobenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-nitrobenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-methoxy-2-nitrobenzoyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1H-indol-4-ylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-[(2,6Dihydroxy-3-naphthalenyl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-(1H-Benzimidazol-5-ylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

4-(1H-Benzotriazol-5-ylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(4-methoxy-2-quinolinyl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine trihydrochloride;

N-[3-[[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepin-4-yl]carbonyl]phenyl]-acetamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-methyl-1-oxo-2-phenylpropyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-[2-(Dimethylamino)benzoyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

4-(3-Ethoxybenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-4-(2-hydroxy[1,1'-biphenyl]-3-ylcarbonyl)-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-4-[2-[(2-hydroxyethyl)thio]benzoyl]-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-methoxy-1-naphthalenyl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-4-[(2-hydroxy-4-quinolyl)-carbonyl]-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2-[[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepin-4-yl]carbonyl]benzamide, dihydrochloride;

N-(1,1-Dimethylethyl)-2-[[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepin-4-yl]carbonyl]benzamide, dihydrochloride;

N-(4-Fluorophenyl)-N'-[3-[[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepin-4-yl]carbonyl]phenyl]urea, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(3-methyl-4-oxo-2-phenyl-4H-benzopyran-8-yl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[3-(trifluoromethoxy)benzoyl]-1H-1,4-benzodiazepine, dihydrochloride;

4-(2-Cyanobenzoyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-[[4-methoxyphenyl)sulfonyl]amino]benzoyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(6-quinolylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(8-quinolylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

4-(Benzo[b]thiophen-2-ylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

4-[[4-(Dimethylamino)-1-naphthalenyl]-carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(1H-purin-6-ylcarbonyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methoxyphenylacetyl)-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(5-methyl-1-phenyl-1H-pyrazol-4-yl)carbonyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-(2-methylphenyl)-1-oxopropyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[(tetrahydro-4-phenyl-2H-pyran-4-yl)carbonyl]-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-(methylphenylamino)benzoyl]-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(4-quinolinylcarbonyl)-1H-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(4-quinolinylcarbonyl)-1H-1,4-benzodiazepine, N-oxide, dihydrochloride;

N-Methyl-N-(2-pyridinylmethyl)-2-[[2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepin-4-yl]carbonyl]benzamide, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-isoquinolinylcarbonyl)-7-phenyl-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-naphthalenylthio)acetyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

4-[3-(3,4-Dimethoxyphenyl)-1-oxopropyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

4-([1,1'-Biphenyl]-4-ylacetyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-naphthalenylacetyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

4-([1,1'-Biphenyl]-2-ylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-phenyl-4-quinolinyl)carbonyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:3);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-pyridinylacetyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:3);

4-(9H-Fluoren-9-ylacetyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

(S)-4-[2-(Dimethylamino)-1-oxo-3-phenylpropyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:3);

(S)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-oxo-4-phenyl-3-oxazolidinyl)acetyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

4-(9-Acridinylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:3);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(3-phenoxybenzoyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[[4'-(trifluoromethyl)[1,1'-biphenyl]-2-yl]carbonyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(4-phenoxybenzoyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-oxo-4-phenylbutyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-phenoxyphenyl)acetyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-[(4-methylphenyl)sulfinyl]benzoyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-[(phenylmethyl)amino]benzoyl]-1H-1,4-benzodiazepine, trifluoroacetate (1:3);

1,2,3,5-Tetrahydro-1-(1H-imidazol-4-yl-methyl)-N,N-diphenyl-4H-1,4-benzodiazepine-4carboxamide, hydrochloride;

1,2,3,5-Tetrahydro-1-(1H-imidazol-4-yl-methyl)-a,7-diphenyl-4H-1,4-benzodiazepine-4-acetic acid, methyl ester, hydrochloride;

4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, monohydrochloride;

(R)-4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

7-Bromo-4-[[2-(dimethylamino)ethyl]sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine, trifluoroacetate (1:2);

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-[(1,2,3,4-tetrahydro-1-quinoliny)carbonyl]-1H-1,4-benzodiazepine, monohydrochloride;

N-Ethyl-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,7-diphenyl-4H-1,4-benzodiazepine-4-carboxamide, monohydrochloride;

4-[(2,3-Dihydro-1H-indol-1-yl)carbonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, monohydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, trihydrochloride;

(R)-4-[[2-(Dimethylamino)ethyl]sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:1);

[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]carbamic acid, cyclohexyl ester, dihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1-methyl-1H-imidazol-5-yl)methyl-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

4-[2-(4-Chlorophenyl)-1,2-dioxoethyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, hydrochloride;

4-(1,2-Dioxopropyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-(4-nitrophenyl)-1,2-dioxoethyl]-7-phenyl-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[2-(4-methoxyphenyl)-1,2-dioxoethyl]-7-phenyl-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(3,3,3-trifluoro-1,2-dioxopropyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:2);

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylacetyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(2-1H-imidazol-4-ylethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

8-[(Cyclohexylcarbonyl)amino]-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-carboxylic acid, methyl ester, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepin-8-yl]-1-piperidinecarboxamide, dihydrochloride;

(R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-carboxylic acid, ethyl ester, hydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-8-yl]cyclohexanecarboxamide, dihydrochloride;

(R)-7-Cyano-4-[[2-(dimethylamino)ethyl]sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[[2-(4-morpholinyl)ethyl]sulfonyl]-3-(phenylmethyl)-4H-1,4-benzodiazepine, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-methoxy-3-methylbenzoyl)-1H-1,4-benzodiazepin-8-yl]cyclohexanecarboxamide, dihydrochloride;

8-[(Cyclohexylcarbonyl)amino]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N-phenyl-1H-1,4-benzodiazepine-4-carboxamide, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-methylphenyl)sulfonyl]-1H-1,4-benzodiazepin-8-yl]cyclohexanamide, dihydrochloride;

N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-methoxyphenyl)carbonyl]-1H-1,4-benzodiazepin-8-yl]cyclohexanamide, dihydrochloride;

(R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-sulfonic acid, ethyl ester, hydrochloride;

(3R)-7-Bromo-1-[cyano(1H-imidazol-4-yl)methyl]-2,3,4,5-tetrahydro-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(3R)-1-[2-Amino-1-(1H-imidazol-4-yl)ethyl]-2,3,4,5-tetrahydro-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(3R)-1-[2-(Dimethylamino)-1-(1H-imidazol-4-yl)ethyl]-2,3,4,5-tetrahydro-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(3R)-1-[2-Amino-1-(1H-imidazol-4-yl)ethyl]-7-bromo-2,3,4,5-tetrahydro-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(3R)-1-[2-(Dimethylamino)-1-(1H-imidazol-4-yl)ethyl]-7-bromo-2,3,4,5-tetrahydro-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Cyano-1,3,4,5-tetrahydro-1-(1-methyl-1H-imidazol-5-ylmethyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-2H-1,4-benzodiazepin-2-one, monohydrochloride;

7-Cyano-1,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-2H-1,4-benzodiazepin-2-one, monohydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(2-phenylethyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-3-[(3-chlorophenyl)methyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Bromo-3-(cyclohexylmethyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-3-[(2-chlorophenyl)methyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

(S)-7-Bromo-3-(cyclohexylmethyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-[(4-methoxyphenyl)methyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

4-Acetyl-7-bromo-3-[(2-chlorophenyl)methyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

4-Acetyl-7-bromo-3-[(3-chlorophenyl)methyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-[(4-hydroxyphenyl)methyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-7-phenyl-3-(3-pyridinylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-8-(hydroxymethyl)-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-8-(phenoxymethyl)-1H-1,4-benzodiazepine, dihydrochloride;

N-Cyclohexyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine-8-carboxamide, dihydrochloride;

N-(Cyclohexylmethyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-1H-1,4-benzodiazepine-8-carboxamide, dihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-naphthalenylcarbonyl)-N-(phenylmethyl)-1H-1,4-benzodiazepine-8-carboxamide, dihydrochloride;

(R)-4-Acetyl-7-[2-[(dimethylamino)methyl]phenyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-4-Acetyl-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-oxobutyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-methyl-1-oxopropyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-pyridinylacetyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(1-methylethyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[(trifluoromethyl)sulfonyl]-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Cyano-4-[(4-fluorophenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Cyano-4-[(3-cyanophenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(1-methyl-1H-imidazol-2-yl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-4-[(3-Bromophenyl)sulfonyl]-7cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-N-[5-[[7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-4-yl]sulfonyl]-4-methyl-2-thiazolyl]acetamide, dihydrochloride;
- 4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, trihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2-phenyl-1,2-dioxoethyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-(4-pyridinyl)-4-[2-(trifluoromethoxy)benzoyl]-1H-1,4-benzodiazepine, trihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-4-(methylsulfonyl)-7-phenyl-3-(phenylmethyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(phenylacetyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

4-(2-Benzothiazolyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-1H-1,4-benzazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-7-(3-pyridinyl)-4-(trifluoroacetyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-7-(3-pyridinyl)-1H-1,4-benzodiazepine, trihydrochloride;

7-Bromo-3-[(1,1-dimethylethoxy)methyl]-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-5H-1,4-benzodiazepin-5-one;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phoxymethyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-2,3,4,5-tetrahydro-3-(hydroxymethyl)-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;

7-Bromo-3-[(1,1-dimethylethoxy)methyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

[7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-8-yl]carbamic acid, 2-methylpropyl ester, trihydrochloride;

[4-Acetyl-7-bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-8-yl]carbamic acid, 2-methylpropyl ester;

N-[4-Acetyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-8-yl]cyclohexanecarboxamide, dihydrochloride;

[7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-8-yl]carbamic acid, 2-methylpropyl ester;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(phenylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, monohydrochloride;

7-Bromo-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-acetamide;

7-Bromo-4-[(dimethylamino)acetyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine;

(R)-7-Bromo-4-(1,2-dioxopropyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(R)-7-Bromo-4-(cyclopropylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine, monohydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1,4-bis(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

7-Bromo-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,N-dimethyl-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-sulfonamide, monohydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, monohydrochloride;

(R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,N-dimethyl-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-carboxamide monohydrochloride;

N,N-Diethyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carboxamide, monohydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(1-phenyl-1H-tetrazol-5-yl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-pyrazinylcarbonyl)-4H-1,4-benzodiazepine, monohydrochloride;

(R)-4-[7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepin-4-yl]-4-oxobutanoic acid, methyl ester, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(4-morpholinocarbonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[[2-(1-pyrrolidinyl)ethyl]sulfonyl]-1H-1,4-benzodiazepine, dihydrochloride;

(S)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-7-phenyl-3-(3-pyridinylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(3-pyridinylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4-(propylsulfonyl)-3-(3-pyridinylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(2-pyridinylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-7-(2-pyrimidinyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[(trifluoromethyl)sulfonyl]-1H-1,4-benzodiazepine, monohydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-4-(trifluoroacetyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-7-(4-pyridinyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(propylsulfonyl)-7-(4-pyridinyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[(3,5-dimethyl-isoxazol-4-yl)sulfonyl]-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-4-[(4-cyanophenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[(2,2,2-trifluoroethyl)sulfonyl]-1H-1,4-benzodiazepine, dihydrochloride;

(R)-[(5-Bromo-2-thienyl)sulfonyl]-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(4-methoxyphenyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

N-[[7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepin-3-ylmethyl]benzamide, dihydrochloride;

(R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,N-dimethyl-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-sulfonamide, hydrochloride;

(R)-7-Cyano-1,2,3,5-tetrahydro-N,N-dimethyl-1-[(1-methyl-1H-imidazol-5-yl)methyl]-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-sulfonamide, hydrochloride;

(R)-7-Chloro-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Chloro-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

- (R)-7-Chloro-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-4-(phenylsulfonyl)-3-phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(pyridin-3-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, tetrahydrochloride;
- (R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-2-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, trihydrochloride;
- (R)-7-Chloro-2,3,4,5-tetrahydro-1-(1-methyl-imidazol-5-ylmethyl)-4-[(2-morpholin-4-yl-ethyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Chloro-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(2-morpholin-4-yl-ethyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Chloro-4-[(dimethylamino)sulfonyl]-1-[(1-methyl-1H-imidazol-5-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Chloro-2,3,4,5-tetrahydro-1-(1-methyl-imidazol-5-ylmethyl)-4-[(4-methyl-piperidin-4-yl-ethyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Bromo-2,3,4,5-tetrahydro-1-(1-methyl-imidazol-5-ylmethyl)-4-[(4-methyl-piperidin-4-yl-ethyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine-4-carboxylic acid, isopropyl ester, hydrochloride;
- (R)-7-Bromo-2,3,4,5-tetrahydro-4-[[2-(1H-imidazol-1-yl)ethyl]sulfonyl]-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(propylsulfonyl)-3-(3-pyridinylmethyl)-1H-1,4-benzodiazepine, hydrochloride;
- 7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepin-5-one, hydrochloride;
- (R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-1-ylacetyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;
- 1,2,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-2-(2-phenylethyl)-3H-1,4-benzodiazepin-3-one;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-2-(2-phenylethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-7-phenyl-3-(4-pyridinylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

- (R)-2,3,4,5-Tetrahydro-1-(1H-imidazol-2-ylmethyl)-4-(phenylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, hydrochloride;
- (R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,N-dimethyl-3-(3-pyridinylmethyl)-4H-1,4-benzodiazepine-4-carboxamide, dihydrochloride;
- (R)-7-Cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N,N-dimethyl-3-(3-pyridinylmethyl)-4H-1,4-benzodiazepine-4-sulfonamide, dihydrochloride;
- (R)-2,3,4,5-Tetrahydro-1-(1-(4cyanophenylmethyl)-imidazol-5ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, hydrochloride;
- (R)-2,3,4,5-Tetrahydro-1-(1-(4-cyanophenylmethyl)-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, hydrochloride;
- (R)-4-Benzoyl-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-3-(pyridin-3-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-3-(pyridin-3-ylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine, trihydrochloride;
- (R)-7-Cyano-2,3,4,5-tetrahydro-1-[(1H-imidazol-4-yl)methyl]-3-(pyridin-3-ylmethyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;
- 2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-7-phenyl-3-(phenylmethyl)-1H-1,4-benzodiazepine;
- 1,2,3,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-N-(1-naphthalenyl)-7-phenyl-4H-1,4-benzodiazepine-4-carboxamide, monohydrochloride;
- (S)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;
- N-[2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(2,3-dimethylbenzoyl)-1H-1,4-benzodiazepin-8-yl]cyclohexanecarboxamide, dihydrochloride;
- (R)-7-Cyano-N-[2-(dimethylamino)ethyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-N-methyl-3-(phenylmethyl)-1H-1,4-benzodiazepine-4-carboxamide, trifluoroacetate (1:2);
- 7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-2-oxo-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;
- (R)-7-Cyano-4-(2-furanylcarbonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:1);

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(4-nitrophenyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[[4-(4-methyl-1-piperazin)phenyl]sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[[4-(dimethylamino)phenyl]sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate;

(R)-7-Bromo-4-[[2-(dimethylamino)ethyl]sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(3-pyridinylsulfonyl)-1H-1,4-benzodiazepine, trihydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-4-yl)methyl]-4-(methylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-4-[[3-(Dimethylamino)propyl]sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trihydrochloride;

4-Butyl-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[[2-(4-morpholinyl)ethyl]sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-4-[[2-(4-morpholinyl)ethyl]sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-1-(1H-imidazol-4-ylmethyl)-4-(4-morpholinylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-1-[(1-methyl-1H-imidazol-5-yl)methyl]-4-[(4-morpholinyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(4-aminophenyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

2,3,4,5-Tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-[(4-pyridylthio)acetyl]-7-phenyl-1H-1,4-benzodiazepine, dihydrochloride;

N-(4-Chlorophenyl)-N'-cyano-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4H-1,4-benzodiazepine-4-imidamide, monohydrochloride;

4-Acetyl-7-bromo-1,2,4,5,1',3'-hexahydro-1-(1H-imidazol-4-ylmethyl)spiro[3H-1,4-benzodiazepine-3,2'-[2H]indene], dihydrochloride;

7-Bromo-4-[3-(dimethylamino)-1-oxopropyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, trifluoroacetate (1:1);

(R)-2,3,4,5-Tetrahydro-1-(1-methyl-1H-imidazol-5-ylmethyl)-4-(phenylsulfonyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine-7-carbonitrile, monohydrochloride;

2,3,4,5-Tetrahydro-1-[(1-methyl-1H-imidazol-5-yl)-methyl]-4-(methyl-sulfonyl)-7-phenyl-3-(pyridin-3-yl-methyl)-1H-1,4-benzodiazepine, hydrochloride (1:1.5), trifluoroacetate (1:0.75) salt;

4-[4-(Fluorophenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-2-(2-phenylethyl)-1H-1,4-benzodiazepine, monohydrochloride;

7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-yl-methyl)-4-(methyl-sulfonyl)-2-(2-phenylethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1-methyl-1H-imidazol-5-ylmethyl)-4-[[2-(1-morpholinyl)ethyl]sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methyl-sulfonyl)-3-(4-bromophenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(methyl-sulfonyl)-3-(thiazol-4-ylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(propyl-sulfonyl)-3-(thiazol-4-ylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(propylsulfonyl)-3-(4-bromophenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(pyridin-3-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, trihydrochloride;

(R)-7-Bromo-2,3,4,5-tetrahydro-1-(1H-1-methyl-imidazol-5-ylmethyl)-3-(pyridin-3-ylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine, dihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(phenyl-sulfonyl)-3-(4-cyanophenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Cyano-4-[(N-methyl-N-phenylmethyl)aminosulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-4-[N-(tetrahydroisoquinoline)sulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(phenylsulfonyl)-3-(2-thienylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

cis-2,3,4,5-Tetrahydro-1,5-bis(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,5-benzodiazepine-2-carboxylic acid ethyl ester-trifluoroacetate (1:2);

(R)-7-Cyano-4-[(N-piperidiny)lsulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine, monohydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-1-methyl-imidazol-5-ylmethyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(pyridin-3-ylmethyl)-4-[[2-(dimethylamino)ethyl]sulfonyl]-1H-1,4-benzodiazepine, trihydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-1-methyl-imidazol-5-ylmethyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine, hydrochloride;

N-(Cyano)-N'-methyl-1,2,3,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-7-phenyl-4H-1,4-benzodiazepine-4-imidamide, hydrochloride;

(R)-7-Cyano-4-[(2-nitrophenyl)-sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenyl-methyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Cyano-4-[(4-methyl-phenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Cyano-4-(butylsulfonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Cyano-4-[(2-trifluoro-methylphenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Cyano-4-[(2-trifluoromethylphenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Cyano-4-[(2-methoxy-carbonylphenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Cyano-4-[(2-methyl-sulfonylphenyl)sulfonyl]-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine, hydrochloride;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(((4-methylnonyl)-phenyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(((4-trifluoromethyl)-phenyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((3-methoxypropyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((3,4-dimethoxyphenyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-((4-fluorophenyl)methyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-4-(N-cyclopropylmethyl-N-propyl)-aminosulfonyl-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-4-[(N,N-(dibutylamino))-sulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine;

(R)-7-Chloro-4-(methanesulfonyl)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-pyrido[3,4-c]-1,4-diazepine;

1,2,3,4-Tetrahydro-7-bromo-4-[(1H-imidazol-4-yl)methyl]-2-phenylmethyl-1-(methylsulfonyl)quinoxaline;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((imidazol-4-yl)methylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-((2-thienyl)methyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-((2-thienyl)methyl)-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((3-methylthiopropyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(((3-methylthio)-propyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(((3-methylsulfonyl)-propyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((2-methylpropyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(cyclopentylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((4,4,4-trifluorobutyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((phenylmethyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[[2-(5-(N-benzoyl)-aminomethyl)-thienyl]-sulfonyl]-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[[2-(1-(3-chloro-5-methyl-pyridin-2-yl))-pyrrolyl]-sulfonyl]-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((4-carboxyphenyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(((3-methyl-1,2,4-oxadiazol-5-yl)-phenyl)-sulfonyl]-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((2,5-dimethoxyphenyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-4-[(N-tetrahydroquinolinyl)sulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-4-(N,N-bis-[1-(2-methylpropyl)amino]-sulfonyl)-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-4-[(N-methyl-N-phenyl)aminosulfonyl]-1-[(1H-imidazol-4-yl)methyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(2-(2,6-dimethylphenyl)-ethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1-(N-phthalimidoethyl)-imidazol-5-ylmethyl)-3-(phenylmethyl)-4-methylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-[(2-(N,N-dimethylamino)-ethyl)-imidazol-5-ylmethyl]-3-(phenylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-[(2-aminoethyl)-imidazol-5-ylmethyl]-3-(phenylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Bromo-4-(methanesulfonyl)-2,3,4,5-tetrahydro-1-[(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-thieno[2,3-e]-1,4-diazepine;

(R)-7-Bromo-4-(methanesulfonyl)-2,3,4,5-tetrahydro-1-[(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-thieno[3,2-e]-1,4-diazepine;

(R)-4-(methanesulfonyl)-2,3,4,5-tetrahydro-1-[(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-8-oxo-pyrimidino[4,5-e]-1,4-diazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-((4-(2-methoxyethoxy)-phenyl)methyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-((4-(2-(dimethylamino)-ethoxy)-phenyl)methyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylsulfonyl)-3-(phenylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylsulfonyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylsulfonyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylsulfonyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-1-phenyl-ethyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-1-phenyl-ethyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-1-phenyl-ethyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-1-phenyl-ethyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-1-phenyl-ethyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-1-phenyl-ethyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-1-phenyl-ethyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-1-phenyl-ethyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-1-phenyl-ethyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-1-phenyl-ethyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-1-phenyl-ethyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-1-phenyl-ethyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-1-phenyl-ethyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-1-phenyl-ethyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-1-phenyl-ethyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-1-phenyl-ethyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-phenylcyclopropyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-phenylcyclopropyl]-4-propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-phenylcyclopropyl]-4-phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(R)-phenylcyclopropyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-phenylcyclopropyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-phenylcyclopropyl]-4-propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-phenylcyclopropyl]-4-phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(R)-[(S)-phenylcyclopropyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-phenylcyclopropyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-phenylcyclopropyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-phenylcyclopropyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(R)-phenylcyclopropyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-phenylcyclopropyl]-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-phenylcyclopropyl]-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-phenylcyclopropyl]-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(S)-[(S)-phenylcyclopropyl]-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[(2-(5-(pyridin-2-yl))-thienyl)-sulfonyl]-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-[(2-(5-(1,2-isoxazol-3-yl))-thienyl)-sulfonyl]-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(3-(1H-imidazol-2-yl)-propyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(3-(1H-imidazol-2-yl)-propyl)-3-(phenylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(3-(1H-imidazol-2-yl)-propyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(3-(1H-imidazol-2-yl)-propyl)-3-(phenylmethyl)-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(2-(1H-imidazol-2-yl)-ethylsulfonyl)-3-(phenylmethyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(2-(1H-imidazol-2-yl)-ethylsulfonyl)-3-(phenylmethyl)-4-(methylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(2-(1H-imidazol-2-yl)-ethylsulfonyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

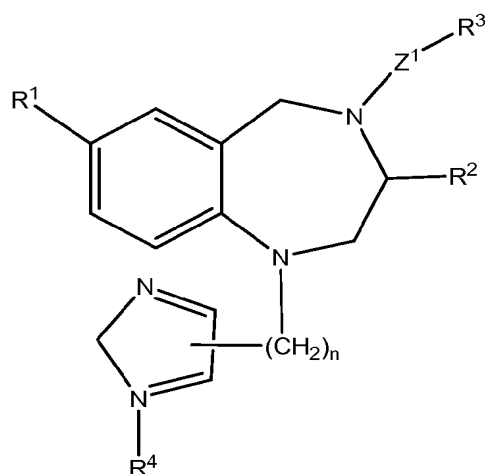
(R)-7-Cyano-2,3,4,5-tetrahydro-1-(2-(1H-imidazol-2-yl)ethylsulfonyl)-3-(phenylmethyl)-4-((2-thienyl)-sulfonyl)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-((1-oxoethyl)-amino)-1H-1,4-benzodiazepine;

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(methanesulfonylamino)-1H-1,4-benzodiazepine; and

(R)-7-Cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(phenylsulfonylamino)-1H-1,4-benzodiazepine.

[00137] In one aspect of the invention is a method of treating a subject with a lysosomal storage disease, the method comprising administering to the subject a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount, wherein R_1 is Cl, Br, CN, optionally substituted phenyl, or optionally substituted 2-,3- or 4-pyridyl; R_2 is optionally substituted lower alkyl, or optionally substituted aralkyl; R_3 and R_5 are each independently optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted heterocyclo; R_4 is hydrogen or lower alkyl; Z_1 is CO, SO₂, CO₂ or SO₂ N(R_5)--; and n is 1 or 2. In one embodiment the compound of the invention has the following substituents:

R_1 is Br, or CN;

R_2 is optionally substituted benzyl;

R_3 is optionally substituted lower alkyl, optionally substituted phenyl, optionally substituted 2-thienyl, or optionally substituted 1-piperidinyl;

R_4 is hydrogen, or methyl;

Z_1 is CO, SO₂, or SO₂ N(R_5)--;

R_5 is optionally substituted lower alkyl or optionally substituted phenyl;

and n is 1.

[00138] In yet another embodiment, the compound of the invention has the following substituents:

R_1 is CN;

R_2 is optionally substituted benzyl;

R_3 is optionally substituted lower alkyl, optionally substituted phenyl, optionally substituted 2-thienyl, or optionally substituted 1-piperidinyl;

R_4 is hydrogen, or methyl;

Z is CO, or SO₂; and

n is 1.

[00139] In yet another embodiment the compound of the invention has the following substituents:

R₁ is CN;

R₂ is benzyl;

R₃ is n-propyl, n-butyl, 3-methoxypropyl, 2-thienyl, 5-bromo-2-thienyl, phenyl, 4-methoxyphenyl, or 1-piperidinyl;

R₄ is hydrogen;

Z is SO₂; and

n is 1.

[00140] In yet another embodiment the compound of the invention is selected from the group consisting of:

(R)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine-7-carbonitrile;

(R)-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-4-(1-oxobutyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine;

(R)-4-[(5-bromo-2-thienyl)sulfonyl]-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenyl methyl)-1H-1,4-benzodiazepine;

(R)-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-yl methyl)-4-[(4-methoxyphenyl)sulfonyl]-3-(phenylmethyl)-1H-1,4-benzodiazepine;

(R)-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenyl methyl)-4-(phenylsulfonyl)-1H-1,4-benzodiazepine;

(R)-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(propylsulfonyl)-1H-1,4-benzodiazepine;

(R)-4-(butylsulfonyl)-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine;

(R)-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(1-piperidinylsulfonyl)-1H-1,4-benzodiazepine;

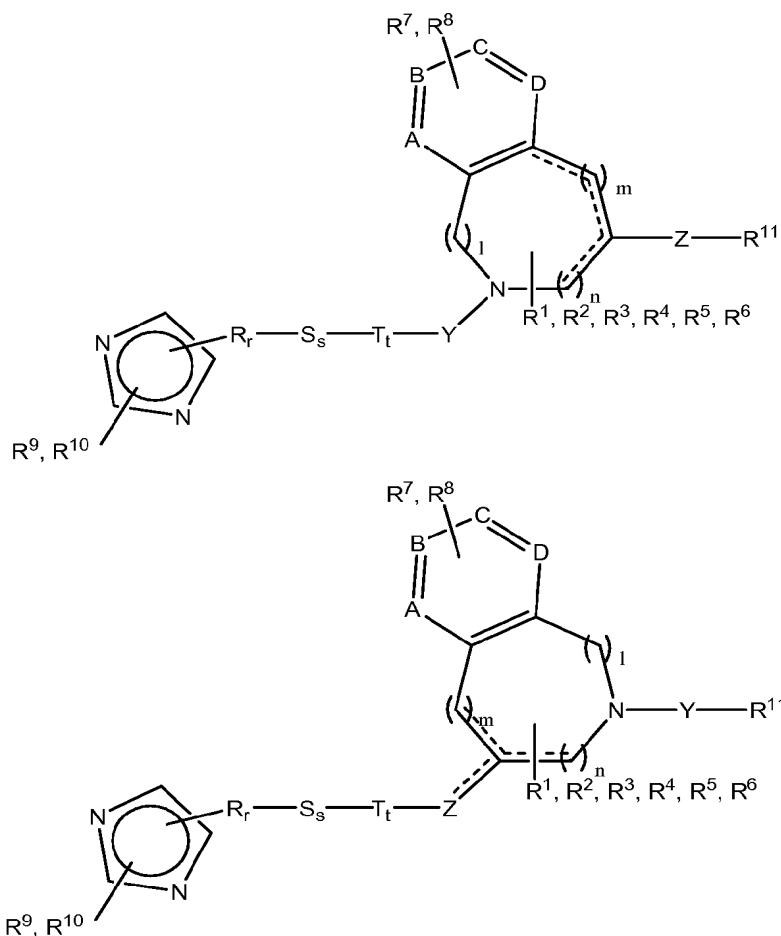
(R)-4-(3-methoxypropylsulfonyl)-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-1H-1,4-benzodiazepine; and

pharmaceutically acceptable salts thereof.

[00141] In certain embodiments of the invention the pharmaceutically acceptable salt is selected from the group consisting of the hydrochloride salt, the methanesulfonic acid salt and the trifluoroacetic acid salt.

[00142] In one embodiment of the invention compound of the invention is (R)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine-7-carbonitrile.

[00143] In another embodiment, the invention provides a method of treating a subject with a lysosomal storage disease, the method comprising administering to the subject a farnesyl transferase inhibitor compound of the formula:

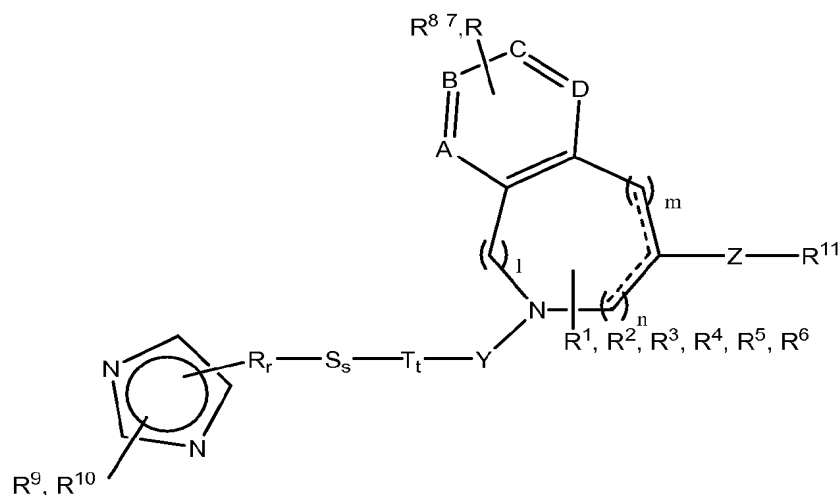


or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount, wherein l, m, r, s and t are 0 or 1; n is 0, 1 or 2; Y is selected from the group consisting of CHR¹², SO₂, SO₃, CO, CO₂, O, NR¹³, SO₂ NR¹⁴, CONR¹⁵, C(NCN), C(NCN)NR¹⁶, NR¹⁷ CO, NR¹⁸ SO₂, CONR¹⁹ NR²⁰, SO₂ NR²¹ NR²², S(O)(NR²³), S(NR²⁴)(NR²⁵), or without Y; Z is selected from the group consisting of CR¹², S, SO, SO₂, SO₃, CO, CO₂, O, NR¹³, SO₂ NR¹⁴, CONR¹⁵, NR²⁶ NR²⁷, ONR²⁸, NR²⁹ O, NR³⁰ SO₂ NR³¹, NR³² SO₂, NR³³ C(NCN), NR³⁴ C(NCN)NR³⁵, NR³⁶ CO, NR³⁷ CONR³⁸, NR³⁹ CO₂, OCONR⁴⁰, S(O)(NR⁴¹), S(NR⁴²)(NR⁴³) or CHR¹²; or without Z; R⁷, R⁸ are selected

from the group consisting of hydrogen, halo, nitro, cyano and U-R⁴⁴; U is selected from the group consisting of S, O, NR⁴⁵, CO, SO, SO₂, CO₂, NR⁴⁶ CO₂, NR⁴⁷ CONR⁴⁸, NR⁴⁹ SO₂, NR⁵⁰ SO₂ NR⁵¹, SO₂ NR⁵², NR⁵³ CO, CONR⁵⁴, PO₂ R⁵⁵ and PO₃ R⁵⁶ or without U; R⁹, R¹⁰, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²², R²³, R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, R²⁹, R³⁰, R³¹, R³², R³³, R³⁴, R³⁵, R³⁶, R³⁷, R³⁸, R³⁹, R⁴⁰, R⁴¹, R⁴², R⁴³, R⁴⁵, R⁴⁶, R⁴⁷, R⁴⁸, R⁴⁹, R⁵⁰, R⁵¹, R⁵², R⁵³, R⁵⁴, R⁵⁵, R⁵⁶, R⁵⁷, R⁵⁸ and R⁵⁹ are selected from the group consisting of hydrogen, lower alkyl, aryl, heterocyclo, substituted alkyl or aryl or substituted heterocyclo; R¹¹ and R⁴⁴ are selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo; R¹, R², R³, R⁴, R⁵ and R⁶ are selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, cyano, carboxy, carbamyl (e.g. CONH₂), substituted carbamyl (where nitrogen may be substituted by groups selected from hydrogen, alkyl, substituted alkyl, aryl or aralkyl, substituted aryl, heterocyclo, substituted heterocyclo), alkoxy carbonyl; any two of R¹, R², R³, R⁴, R⁵ and R⁶ can join to form a cycloalkyl group; any two of R¹, R², R³, R⁴, R⁵ and R⁶ together can be oxo, except when the carbon atom bearing the substituent is part of a double bond; R, S and T are selected from the group consisting of CH₂, CO and CH(CH₂)_p Q wherein Q is NR⁵⁷ R⁵⁸, OR⁵⁹, or CN; and p is 0, 1 or 2; A, B and C are carbon, oxygen, sulfur or nitrogen; D is carbon, oxygen, sulfur or nitrogen or without D; and with the provisos:

1. When l and m are both 0, n is not 0;
2. R¹¹ may be hydrogen except when Z is SO, or when Z is O, NR¹³ or S and the carbon to which it is attached is part of a double bond or when Y is SO₂, CO₂, NR¹⁸ SO₂, S(O)(NR²³), or S(NR²⁴)(NR²⁵);
3. R⁴⁴ may be hydrogen except when U is SO, SO₂, NR⁴⁶ CO₂ or NR⁴⁹ SO₂.

[00144] In one embodiment the compound has the formula:



wherein

r , s and t are 0 or 1;

l is 0; m is 1; n is 1;

Y is selected from the group consisting of CHR^{12} , SO_2 , SO_3 , CO_2 , O , NR^{13} , $SO_2 NR^{14}$, $CONR^{15}$, $C(NCN)$, $C(NCN)NR^{16}$, $NR^{17} CO$, $NR^{18} SO_2$, $CONR^{19} NR^{20}$, $SO_2 NR^{21} NR^{22}$, $S(O)(NR^{23})$, $S(NR^{24})(NR^{25})$, or without Y ;

Z is selected from the group consisting of S , SO , SO_2 , SO_3 , CO , CO_2 , O , NR^{13} , $SO_2 NR^{14}$, $CONR^{15}$, $NR^{26} NR^{27}$, ONR^{28} , $NR^{29} O$, $NR^{30} SO_2 NR^{31}$, $NR^{32} SO_2$, $NR^{33} C(NCN)$, $NR^{34} C(NCN)NR^{35}$, $NR^{36} CO$, $NR^{37} CONR^{38}$, $NR^{39} CO_2$, $OCONR^{40}$, $S(O)(NR^{41})$, or $S(NR^{42})(NR^{43})$;

R^7 , R^8 are selected from the group consisting of hydrogen, halo, nitro, cyano and $U-R^{44}$;

U is selected from the group consisting of S , O , NR^{45} , CO , SO , SO_2 , CO_2 , $NR^{46} CO_2$, $NR^{47} CONR^{48}$, $NR^{49} SO_2$, $NR^{50} SO_2 NR^{51}$, $SO_2 NR^{52}$, $NR^{53} CO$, $CONR^{54}$, $PO_2 R^{55}$ and $PO_3 R^{56}$ or without U ;

R^9 , R^{10} , R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} , R^{19} , R^{20} , R^{21} , R^{22} , R^{23} , R^{24} , R^{25} , R^{26} , R^{27} , R^{28} , R^{29} , R^{30} , R^{31} , R^{32} , R^{33} , R^{34} , R^{35} , R^{36} , R^{37} , R^{38} , R^{39} , R^{40} , R^{41} , R^{42} , R^{43} , R^{45} , R^{46} , R^{47} , R^{48} , R^{49} , R^{50} , R^{51} , R^{52} , R^{53} , R^{54} , R^{55} , R^{56} , R^{57} , R^{58} and R^{59} are selected from the group consisting of hydrogen, lower alkyl, aryl, heterocyclo, substituted alkyl or aryl;

R^{11} and R^{44} are selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo;

R^1 , R^2 , R^3 , R^4 , R^5 and R^6 are selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl,

cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, cyano, alkoxycarbonyl, carboxy, carbamyl, substituted carbamyl wherein substituents on the nitrogen of the substituted carbamyl are selected hydrogen, alkyl, substituted alkyl, aryl or aralkyl, substituted aryl, heterocyclo, substituted heterocyclo; any two of R^1 , R^2 , R^3 , R^4 , R^5 and R^6 can join to form a cycloalkyl group; any two of R^1 , R^2 , R^3 , R^4 , R^5 and R^6 together can be oxo, except when the carbon atom bearing the substituent is part of a double bond;

R, S and T are selected from the group consisting of CH_2 , and $CH(CH_2)_p$ Q wherein Q is $NR^{57}R^{58}$, OR^{59} , or CN;

wherein p is 0, 1 or 2; and

A, B, C and D are carbon; its enantiomers, diastereomers, pharmaceutically acceptable salts and solvates thereof;

with the provisos that:

1. R^{11} may be hydrogen except when Z is SO, or when Z is O, NR^{13} or S and the carbon to which it is attached is part of a double bond or when Y is SO_2 , CO_2 , $NR^{18}SO_2$, $S(O)(NR^{23})$, or $S(NR^{24})(NR^{25})$; and
2. R^{44} may be hydrogen except when U is SO, SO_2 , $NR^{46}CO_2$ or $NR^{49}SO_2$.

[00145] In another embodiment the compound has the following substituents:

l, m, r, s and t are 0 or 1; n is 1 or 2;

Y is CHR^{12} , SO_2 , SO_3 , CO_2 , SO_2NR^{14} , $CONR^{15}$ or without Y;

Z is SO_2 , SO_3 , CO, CO_2 , NR^{13} , SO_2NR^{14} , $CONR^{15}$, $NR^{30}SO_2NR^{31}$, $NR^{32}SO_2$, $NR^{36}CO$, $NR^{37}CONR^{38}$, or $NR^{39}CO_2$.

[00146] In another embodiment the compound has the following substituents:

l, r, s, and t is 0;

Y is CHR^{12} , SO_2 , SO_2NR^{14} , or $CONR^{15}$ or without Y; and

Z is SO_2 , SO_3 , CO, CO_2 , SO_2NR^{14} , $CONR^{15}$, $NR^{30}SO_2NR^{31}$, $NR^{32}SO_2$, $NR^{36}CO$, NR^{37} or $CONR^{38}$, $NR^{39}CO_2$.

In yet another embodiment the compound has the following substituents:

R^7 , R^8 is halogen, nitro, cyano or $U-R^{44}$ wherein U is S, O, $NR^{46}CO_2$, $NR^{47}CONR^{48}$, R^{44} is hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo or substituted heterocyclo, R^{46} and R^{47} is hydrogen, lower alkyl, aryl substituted alkyl or aryl.

[00147] In yet another embodiment the the salt is of an organic or inorganic acid.

[00148] In yet another embodiment the salt is of hydrogen chloride, hydrogen bromide, methanesulfonic acid, hydroxyethanesulfonic acid, sulfuric acid, acetic acid, trifluoroacetic acid, maleic acid, benzenesulfonic acid, toluenesulfonic acid, nitric acid, phosphoric acid, boric acid, tartaric acid, citric acid, succinic acid, benzoic acid, ascorbic acid or salicylic acid.

[00149] In yet another embodiment the compound is:

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-1-naphthalenesulfonamide, dihydrochloride;

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-1-naphthalenecarboxamide, dihydrochloride;

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-(phenylmethyl)methanesulfonamide, dihydrochloride;

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]benzenesulfonamide, dihydrochloride;

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-(phenylmethyl)acetamide, dihydrochloride;

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-(4-methoxyphenyl)methylmethanesulfonamide, monohydrochloride;

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(4-methylphenyl)methyl]methanesulfonamide monohydrochloride;

N-[6-cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(3-methylphenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(2-methylphenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-(phenylethyl)benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(2-ethoxyphenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-(phenylmethyl)benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(2,3-dimethoxyphenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(3,5-dimethylphenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(1-naphthalenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(2-thiophene)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(2,5-dimethylphenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(3-thiophene)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(3-chlorophenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(2-fluorophenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(3-pyridyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-[[1-(methyl)-1H-imidazol-5-yl]methyl]-3-quinoliny]-N-(phenylmethyl)benzenesulfonamide monohydrochloride;

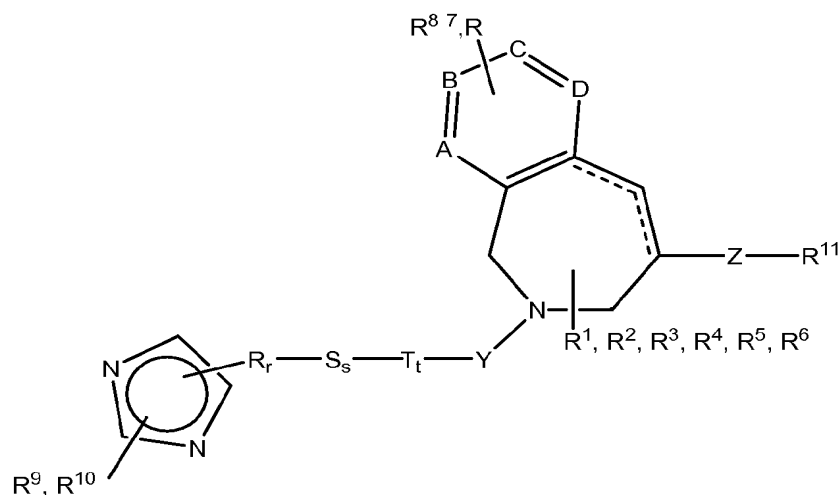
N-[6-Cyano-1,2,3,4-tetrahydro-1-[[1-(methyl)-1H-imidazol-5-yl]methyl]-3-quinoliny]-N-[(3-thiophenemethyl)]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-(phenylmethyl)methanesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-[[1-(methyl)-1H-imidazol-5-yl]methyl]-3-quinoliny]-N-(phenylmethyl)methanesulfonamide monohydrochloride;

(R)-N-[6-Cyano-1,2,3,4-tetrahydro-1-[[1-(methyl)-1H-imidazol-5-yl]methyl]-3-quinoliny]-N-(phenylmethyl)benzenesulfonamide monohydrochloride.

[00150] In yet another embodiment, the invention is a method of treating a subject with a lysosomal storage disease, the method comprising administering to the subject a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount, wherein Y is selected from the group consisting of CHR^{12} , SO_2 , SO_3 , CO , CO_2 , O , NR^{13} , $\text{SO}_2 \text{NR}^{14}$, CONR^{15} , $\text{C}(\text{NCN})$, $\text{C}(\text{NCN})\text{NR}^{16}$, $\text{NR}^{17} \text{CO}$, $\text{NR}^{18} \text{SO}_2$, $\text{CONR}^{19} \text{NR}^{20}$, $\text{SO}_2 \text{NR}^{21} \text{NR}^{22}$, $\text{S}(\text{O})(\text{NR}^{23})$, and $\text{S}(\text{NR}^{24})(\text{NR}^{25})$, or without Y; Z is selected from the group consisting of S , SO , SO_2 , SO_3 , CO , CO_2 , O , NR^{13} , $\text{SO}_2 \text{NR}^{14}$, CONR^{15} , $\text{NR}^{26} \text{NR}^{27}$, ONR^{28} , $\text{NR}^{29} \text{O}$, $\text{NR}^{30} \text{SO}_2 \text{NR}^{31}$, $\text{NR}^{32} \text{SO}_2$, $\text{NR}^{33} \text{C}(\text{NCN})$, $\text{NR}^{34} \text{C}(\text{NCN})\text{NR}^{35}$, $\text{NR}^{36} \text{CO}$, $\text{NR}^{37} \text{CONR}^{38}$, $\text{NR}^{39} \text{CO}_2$, OCONR^{40} , $\text{S}(\text{O})(\text{NR}^{41})$, and $\text{S}(\text{NR}^{42})(\text{NR}^{43})$; R^7 and R^8 are selected from the group consisting of hydrogen, halo, nitro, cyano and U--R^{44} ; U is selected from the group consisting of S , O , NR^{45} , CO , SO , SO_2 , CO_2 , $\text{NR}^{46} \text{CO}_2$, $\text{NR}^{47} \text{CONR}^{48}$, $\text{NR}^{49} \text{SO}_2$, $\text{NR}^{50} \text{SO}_2 \text{NR}^{51}$, $\text{SO}_2 \text{NR}^{52}$, $\text{NR}^{53} \text{CO}$, CONR^{54} , $\text{PO}_2 \text{R}^{55}$ and $\text{PO}_3 \text{R}^{56}$ or without U; R^9 , R^{10} , R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} , R^{19} , R^{20} , R^{21} , R^{22} , R^{23} , R^{24} , R^{25} , R^{26} , R^{27} , R^{28} , R^{29} , R^{30} , R^{31} , R^{32} , R^{33} , R^{34} , R^{35} , R^{36} , R^{37} , R^{38} , R^{39} , R^{40} , R^{41} , R^{42} , R^{43} , R^{44} , R^{45} , R^{46} , R^{47} , R^{48} , R^{49} , R^{50} , R^{51} , R^{52} , R^{53} , R^{54} , R^{55} , R^{56} , R^{57} , R^{58} , and R^{59} are selected from the group consisting of hydrogen, lower alkyl, aryl, heterocyclo, substituted alkyl and aryl; R^{11} and R^{44} are selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, and substituted heterocyclo; R^1 , R^2 , R^3 , R^4 , R^5 and R^6 are selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, cyano, alkoxycarbonyl, carboxy, carbamyl, and substituted carbamyl wherein substituents on the nitrogen of the substituted carbamyl are selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, aralkyl, substituted aryl, heterocyclo, and substituted heterocyclo; any two of R^1 , R^2 , R^3 , R^4 , R^5 and

R^6 can join to form a cycloalkyl group; any two of R^1 , R^2 , R^3 , R^4 , R^5 and R^6 together can be oxo, except when the carbon atom bearing the substituent is part of a double bond; R, S and T are selected from the group consisting of CH_2 and $CH(CH_2)_p$ Q wherein Q is $NR^{57}R^{58}$, OR^{59} , or CN; p is 0, 1 or 2; and A, B, C and D are carbon; its enantiomer, diastereomer, pharmaceutically acceptable salt or solvate thereof; with the provisos that:

1. R^{11} may be hydrogen except when Z is SO, or when Z is O, NR^{13} or S and the carbon to which it is attached is part of a double bond or when Y is SO_2 , CO_2 , $NR^{18}SO_2$, $S(O)(NR^{23})$, or $S(NR^{24})(NR^{25})$; and
2. R^{44} may be hydrogen except when U is SO, SO_2 , $NR^{46}CO_2$ or $NR^{49}SO_2$.

[00151] In certain embodiments, r, s and t are 0 or 1;

Y is CHR^{12} , SO_2 , SO_3 , CO, CO_2 , SO_2NR^{14} , $CONR^{15}$ or without Y;

Z is CR^{12} , SO_2 , SO_3 , CO, CO_2 , NR^{13} , SO_2NR^{14} , $CONR^{15}$, $NR^{30}SO_2NR^{31}$, $NR^{32}SO_2$, $NR^{36}CO$, $NR^{37}CONR^{38}$, $NR^{39}CO_2$ or without Z.

[00152] In one embodiment of this aspect of the invention, r, s and t are 0 or 1;

Y is CHR^{12} , SO_2 , SO_3 , CO, CO_2 , SO_2NR^{14} , $CONR^{15}$ or without Y;

Z is CR^{12} , SO_2 , SO_3 , CO, CO_2 , NR^{13} , SO_2NR^{14} , $CONR^{15}$, $NR^{30}SO_2NR^{31}$, $NR^{32}SO_2$, $NR^{36}CO$, $NR^{37}CONR^{38}$, $NR^{39}CO_2$ or without Z.

[00153] In yet another embodiment, r, s, and t is 0; Y is CHR^{12} , SO_2 , CO, SO_2NR^{14} , or $CONR^{15}$ or without Y; and Z is CR^{12} , SO_2 , SO_3 , CO, CO_2 , SO_2NR^{14} , $CONR^{15}$, $NR^{30}SO_2NR^{31}$, $NR^{32}SO_2$, $NR^{36}CO$, $NR^{37}CONR^{38}$, $NR^{39}CO_2$ or without Z.

[00154] In yet another embodiment, R^7 , R^8 is halogen, nitro, cyano or $U-R^{44}$ wherein U is S, O, $NR^{46}CO_2$, $NR^{47}CONR^{48}$, R^{44} is hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo or substituted heterocyclo, R^{46} and R^{47} is hydrogen, lower alkyl, aryl substituted alkyl or aryl.

[00155] In one embodiment the compound of the invention is selected from the group consisting of:

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-1-naphthalenesulfonamide, dihydrochloride;

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-1-naphthalenecarboxamide, dihydrochloride;

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-(phenylmethyl)methanesulfonamide, dihydrochloride;

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]benzenesulfonamide, dihydrochloride;

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-(phenylmethyl)acetamide, dihydrochloride;

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-(4-methoxyphenyl)methyl]methanesulfonamide, monohydrochloride;

N-[6-bromo-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(4-methylphenyl)methyl]methanesulfonamide monohydrochloride;

N-[6-cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(3-methylphenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(2-methylphenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-(phenylethyl)benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(2-ethoxyphenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-(phenylmethyl)benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(2,3-dimethoxyphenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(3,5-dimethylphenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(1-naphthalenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(2-thiophene)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(2,5-dimethylphenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(3-thiophene)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(3-chlorophenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(2-fluorophenyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-[(3-pyridyl)methyl]benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-[[1-(methyl)-1H-imidazol-5-yl]methyl]-3-quinoliny]-N-(phenylmethyl)benzenesulfonamide monohydrochloride;

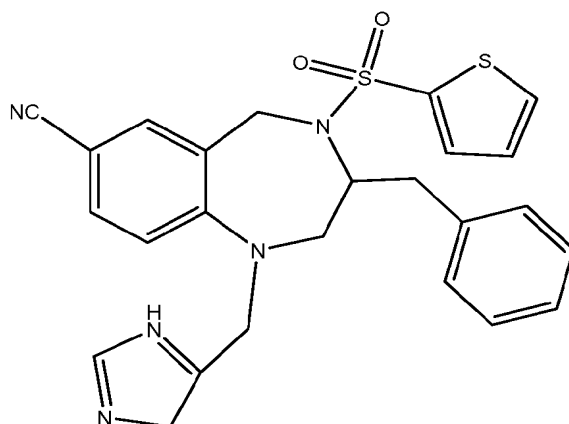
N-[6-Cyano-1,2,3,4-tetrahydro-1-[[1-(methyl)-1H-imidazol-5-yl]methyl]-3-quinoliny]-N-[(3-thiophenemethyl)benzenesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-quinoliny]-N-(phenylmethyl)methanesulfonamide monohydrochloride;

N-[6-Cyano-1,2,3,4-tetrahydro-1-[[1-(methyl)-1H-imidazol-5-yl]methyl]-3-quinoliny]-N-(phenylmethyl)methanesulfonamide monohydrochloride;

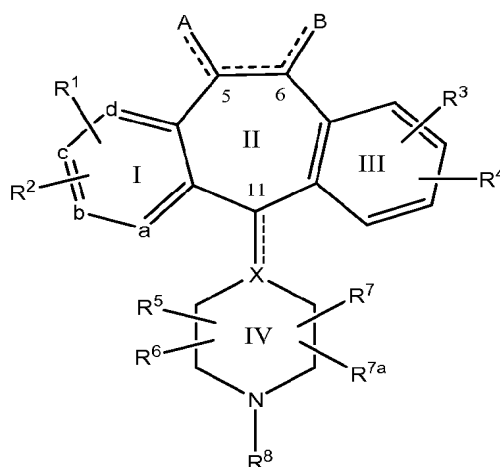
(R)-N-[6-Cyano-1,2,3,4-tetrahydro-1-[[1-(methyl)-1H-imidazol-5-yl]methyl]-3-quinoliny]-N-(phenylmethyl)benzenesulfonamide monohydrochloride.

[00156] In another embodiment, the invention is a method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject with a lysosomal storage disease a farnesyl transferase inhibitor of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount.

[00157] In certain embodiments, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount, wherein:

one of a, b, c and d represents N or N^+O^- , and the remaining a, b, c, and d groups represent carbon, wherein each carbon has an R^1 or R^2 group bound to said carbon; or

each of a, b, c, and d is carbon, wherein each carbon has an R^1 or R^2 group bound to said carbon;

the dotted line (---) represents optional bonds;

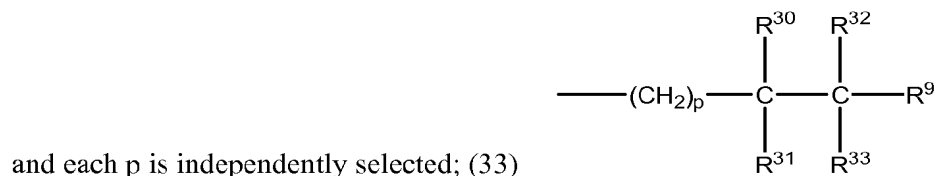
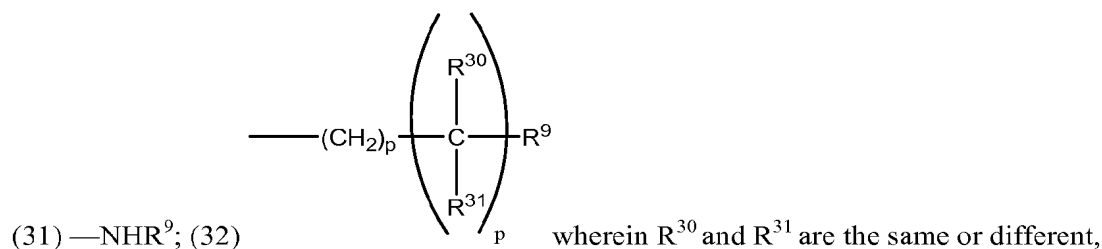
X represents N or CH when the optional bond to C11 is absent, and represents C when the optional bond to C11 is present;

when the optional bond is present between carbon atom 5 and carbon atom 6 then there is only one A substituent bound to C-5 and there is only one B substituent bound to C-6 and A or B is other than H;

when the optional bond is not present between carbon atom 5 and carbon atom 6 then there are two A substituents bound to C-5, wherein each A substituent is independently selected, and two B substituents bound to C-6, wherein each B substituent is independently selected, and wherein at least one of the two A substituents or one of the two B substituents are H, and wherein at least one of the two A substituents or one of the two B substituents is other than H;

A and B are independently selected from the group consisting of: (1) H; (2) $-R^9$; (3) $-R^9-C(O)-R^9$; (4) $-R^9-CO_2-R^{9a}$; (5) $-(CH_2)_pR^{26}$; (6) $-C(O)N(R^9)_2$, wherein each R^9 is the same or different; (7) $-C(O)NHR^9$; (8) $-C(O)NH-CH_2-C(O)-NH_2$; (9) $-C(O)NHR^{26}$; (10) $-(CH_2)_pC(R^9)-O-R^{9a}$; (11) $-(CH_2)_p(R^9)_2$, wherein each R^9 is the same or different; (12) $-(CH_2)_pC(O)R^9$; (13) $-(CH_2)_pC(O)R^{27}$; (14) $-(CH_2)_pC(O)N(R^9)_2$, wherein each R^9 is the same or different; (15) $-(CH_2)_pC(O)NH(R^9)$; (16) —

(CH₂)_pC(O)N(R²⁶)₂, wherein each R²⁶ is the same or different; (17) —(CH₂)_pN(R⁹)—R^{9a}; (18) —(CH₂)_pN(R²⁶)₂, wherein R²⁶ is the same or different; (19) —(CH₂)_pNHC(O)R⁵; (20) —(CH₂)_pNHC(O)₂R⁵⁰; (21) —(CH₂)_pN(C(O)R^{27a})₂ wherein each R^{27a} is the same or different; (22) —(CH₂)_pNR⁵¹C(O)R²⁷; (23) —(CH₂)_pNR⁵¹C(O)R²⁷ wherein R⁵¹ is not H, and R⁵¹ and R²⁷ taken together with the atoms to which they are bound form a 5 or 6 membered heterocycloalkyl ring consisting; (24) —(CH₂)_pNR⁵¹C(O)NR²⁷; (25) —(CH₂)_pNR⁵¹C(O)NR²⁷ wherein R⁵¹ is not H, and R⁵¹ and R²⁷ taken together with the atoms to which they are bound form a 5 or 6 membered heterocycloalkyl ring; (26) —(CH₂)_pNR⁵¹C(O)N(R^{27a})₂, wherein each R^{27a} is the same or different; (27) —(CH₂)_pNHSO₂N(R⁵¹)₂, wherein each R⁵¹ is the same or different; (28) —(CH₂)_pNHCO₂R⁵⁰; (29) —(CH₂)_pNC(O)NHR⁵¹; (30) —(CH₂)_pCO₂R⁵¹;

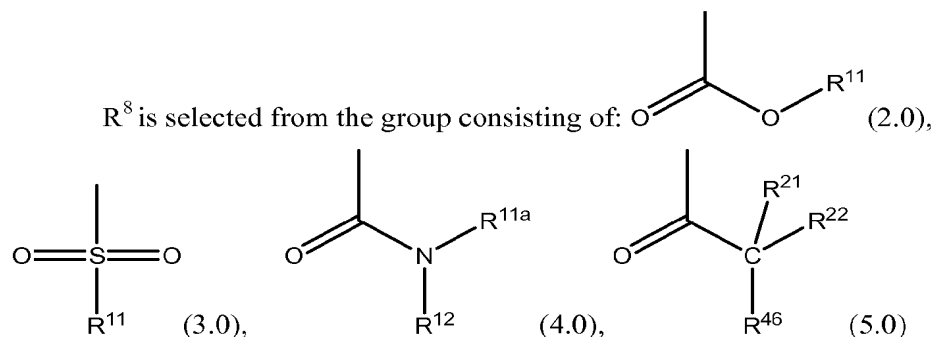


wherein R³⁰, R³¹, R³² and R³³ are the same or different; (34)-alkenyl-CO₂R^{9a}; (35)-alkenyl-C(O)R^{9a}; (36)-alkenyl-CO₂R⁵¹; (37)- alkenyl-C(O)—R^{27a}; (38) (CH₂)_p-alkenyl-CO₂—R⁵¹; (37) —(CH₂)_pC=NOR⁵¹; and (39) —(CH₂)_p-phthalimid; p is 0, 1, 2, 3 or 4;

each R¹ and R² is independently selected from the group consisting of: (1) H; (2) Halo; (3) —CF₃; (4) —OR¹⁰; (5) —COR¹⁰; (6) —SR¹⁰; (7) —S(O)_tR¹⁵ wherein t is 0, 1 or 2; (8) —N(R¹⁰)₂; (9) —NO₂; (10) —OC(O)R¹⁰; (11) —CO₂R¹⁰; (12) —OCO₂R¹⁵; (13) —CN; (14) —NR¹⁰COOR¹⁵; (15) —SR¹⁵C(O)OR¹⁵; (16) —SR¹⁵N(R¹³)₂ provided that R¹⁵ in —SR¹⁵N(R¹³)₂ is not —CH₂ and wherein each R is independently selected from the group consisting of: H and —C(O)OR¹⁵; (17) benzotriazol-1-yloxy; (18) tetrazol-5-ylthio; (19) substituted tetrazol-5-ylthio; (20) alkynyl; (21) alkenyl; and (22) alkyl, said alkyl or alkenyl group optionally being substituted with halogen, —OR¹⁰ or —CO₂R¹⁰;

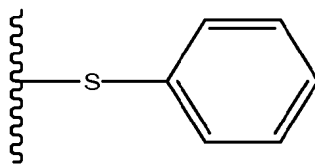
R³ and R⁴ are the same or different and each independently represent H, and any of the substituents of R¹ and R²;

R^5 , R^6 , R^7 and R^{7a} each independently represent: H, $-\text{CF}_3$, $-\text{COR}^{10}$, alkyl or aryl, said alkyl or aryl optionally being substituted with $-\text{S}(\text{O})_t\text{R}^{15}$, $-\text{NR}^{10}\text{COOR}^{15}$, $-\text{C}(\text{O})\text{R}^{10}$; or $-\text{CO}_2\text{R}^{10}$, or R^5 is combined with R^6 to represent $=\text{O}$ or $=\text{S}$;



R^9 is selected from the group consisting of: (1) unsubstituted heteroaryl; (2) substituted heteroaryl; (3) arylalkoxy; (4) substituted arylalkoxy; (5) heterocycloalkyl; (6) substituted heterocycloalkyl; (7) heterocycloalkylalkyl; (8) substituted heterocycloalkylalkyl; (9) unsubstituted heteroarylalkyl; (10) substituted heteroarylalkyl; (11) unsubstituted heteroarylalkenyl; (12) substituted heteroarylalkenyl; (13) unsubstituted heteroarylalkynyl and (14) substituted heteroarylalkynyl;

wherein said substituted R^9 groups are substituted with one or more substituents selected from the group consisting of: (1) $-\text{OH}$; (2) $-\text{CO}_2\text{R}^{14}$; (3) $-\text{CH}_2\text{OR}^{14}$; (4) halogen; (5) alkyl; (6) amino; (7) trityl; (8) heterocycloalkyl; (9) cycloalkyl; (10) arylalkyl; (11)



heteroaryl; (12) heteroarylalkyl and

wherein R^{14} is independently selected from the group consisting of: H; alkyl; aryl, arylalkyl, heteroaryl and heteroarylalkyl;

R^{9a} is selected from the group consisting of: alkyl and arylalkyl;

R^{10} is selected from the group consisting of: H; alkyl; aryl and arylalkyl;

R^{11} is selected from the group consisting of: (1) alkyl; (2) substituted alkyl; (3) unsubstituted aryl; (4) substituted aryl; (5) unsubstituted cycloalkyl; (6) substituted cycloalkyl; (7) unsubstituted heteroaryl; (8) substituted heteroaryl; (9) heterocycloalkyl; and (10) substituted heterocycloalkyl; wherein said substituted alkyl, substituted cycloalkyl, and substituted heterocycloalkyl R^{11} groups are substituted with one or more substituents selected

from the group consisting of: (1) —OH; (2) fluoro; and (3) alkyl; and wherein said substituted aryl and substituted heteroaryl R^{11} groups are substituted with one or more substituents independently selected from the group consisting of: (1) —OH; (2) halogen; and (3) alkyl;

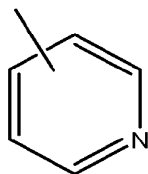
R^{11a} is selected from the group consisting of: (1) H; (2) OH; (3) alkyl; (4) substituted alkyl; (5) unsubstituted aryl; (6) substituted aryl; (7) unsubstituted cycloalkyl; (8) substituted cycloalkyl; (9) unsubstituted heteroaryl; (10) substituted heteroaryl; (11) heterocycloalkyl; and (12) substituted heterocycloalkyl; wherein said substituted alkyl, substituted cycloalkyl, and substituted heterocycloalkyl R^{11a} groups are substituted with one or more substituents independently selected from the group consisting of: (1) —OH; (2) —CN; (3) —CF₃; (4) fluoro; (5) alkyl; (6) cycloalkyl; (7) heterocycloalkyl; (8) arylalkyl; (9) heteroarylalkyl; (10) alkenyl and (11) heteroalkenyl; and wherein said substituted aryl and substituted heteroaryl R^{11a} groups have one or more substituents independently selected from the group consisting of: (1) —OH; (2) —CN; (3) —CF₃; (4) halogen; (5) alkyl; (6) cycloalkyl; (7) heterocycloalkyl; (8) arylalkyl; (9) heteroarylalkyl; (10) alkenyl; and (11) heteroalkenyl;

R^{12} is selected from the group consisting of: H, alkyl, piperidine Ring V, cycloalkyl, and -alkyl-(piperidine Ring V);

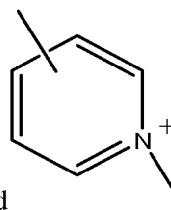
R^{15} is selected from the group consisting of: alkyl and aryl;

R^{21} , R^{22} and R^{46} are independently selected from the group consisting of: (1) —H; (2) alkyl; (3) unsubstituted aryl; (4) substituted aryl substituted with one or more substituents independently selected from the group consisting of: alkyl, halogen, CF₃ and OH; (5) unsubstituted cycloalkyl; (6) substituted cycloalkyl substituted with one or more substituents independently selected from the group consisting of: alkyl, halogen, CF₃ and OH; (7)

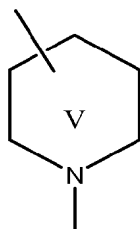
heteroaryl of the formula,



and



and (8) heterocycloalkyl of



the formula: R^{44} wherein R^{44} is selected from the group consisting of: (a) $-H$, (b) alkyl; (c) alkylcarbonyl; (d) alkyloxy carbonyl; (e) haloalkyl; and (f) $-C(O)NH(R^{51})$;

R^{26} is selected from the group consisting of: (1) H ; (2) alkyl; (3) alkoxy; (4) $-CH_2-CN$; (5) R^9 ; (6) $-CH_2CO_2H$; (7) $-C(O)alkyl$; and (8) CH_2CO_2alkyl ;

R^{27} is selected from the group consisting of: (1) $-H$; (2) $-OH$; (3) alkyl; and (4) alkoxy;

R^{27a} is selected from the group consisting of: (1) alkyl; and (2) alkoxy;

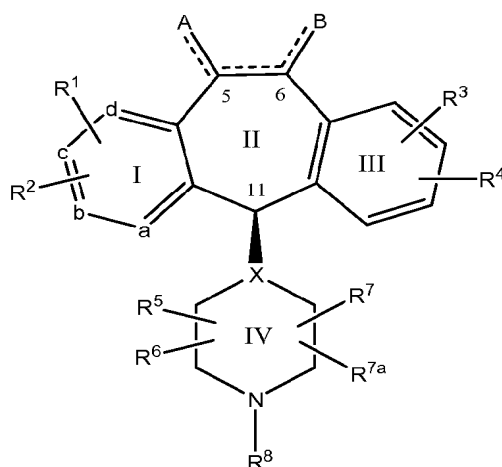
R^{30} , R^{31} , R^{32} and R^{33} are independently selected from the group consisting of: (1) $-H$; (2) $-OH$; (3) $=O$; (4) alkyl; (5) aryl (e.g. phenyl); (6) arylalkyl (e.g. benzyl); (7) $-OR^{9a}$; (8) $-NH_2$; (9) $-NHR^{9a}$; and (10) $-N(R^{9a})_2$ wherein each R^{9a} is independently selected;

R^{50} is selected from the group consisting of: (1) alkyl; (2) unsubstituted heteroaryl; (3) substituted heteroaryl; and (4) amino; wherein said substituents on said substituted R^{50} groups are independently selected from the group consisting of: alkyl, halogen, and $-OH$;

R^{51} is selected from the group consisting of: H , and alkyl;

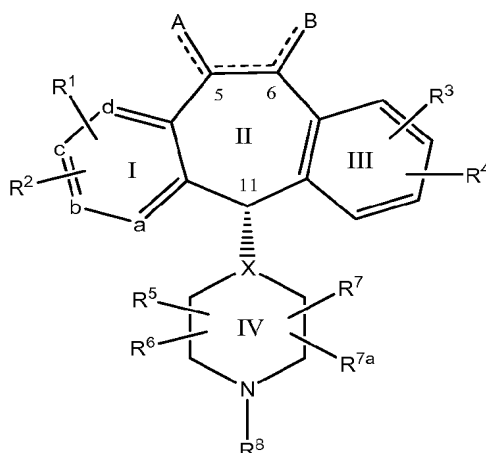
provided that a ring carbon atom adjacent to a ring heteroatom in a substituted heterocycloalkyl moiety is not substituted with a heteroatom or a halo atom; and provided that a ring carbon atom, that is not adjacent to a ring heteroatom, in a substituted heterocycloalkyl moiety, is not substituted with more than one heteroatom; and provided that a ring carbon atom, that is not adjacent to a ring heteroatom, in a substituted heterocycloalkyl moiety, is not substituted with a heteroatom and a halo atom; and provided that a ring carbon in a substituted cycloalkyl moiety is not substituted with more than one heteroatom; and provided that a carbon atom in a substituted alkyl moiety is not substituted with more than one heteroatom; and provided that the same carbon atom in a substituted alkyl moiety is not substituted with both heteroatoms and halo atoms.

[00158] In one embodiment, the compound has the formula:



X=CH or N; B is H when the optional bond is present between C-5 and C-6, and when the optional bond between C-5 and C-6 is absent then each B is H.

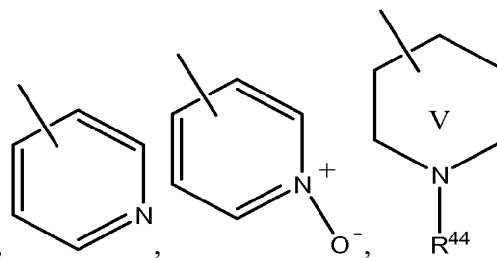
[00159] In another embodiment, the compound has the formula:



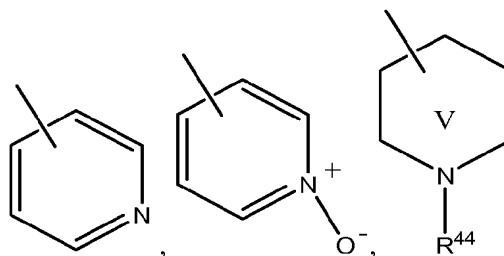
X=CH or N; A is H when the optional bond is present between C-5 and C-6, and when the optional bond between C-5 and C-6 is absent then each A is H.

In any embodiment of this aspect of the invention, R¹ to R⁴ each may be independently selected from H or halo. R⁵ to R⁷ may be H. In one embodiment, a may be N and the remaining b, c and d substituents may be carbon. In another embodiment, a, b, c, and d may be carbon. The optional bond between C-5 and C-6 may be present. Alternatively, the optional bond between C-5 and C-6 may be absent. R⁸ may be group 2.0, or 4.0. One of A and B may be H and the other may be R⁹. R⁹ may be selected from the group consisting of: (1) heterocycloalkylalkyl of the formula —(CH₂)_n-heterocycloalkyl; (2) substituted heterocycloalkylalkyl of the formula —(CH₂)_n-substituted heterocycloalkyl; (3) unsubstituted heteroarylalkyl of the formula —(CH₂)_n-heteroaryl; and (4) substituted heteroarylalkyl of the

formula $-(CH_2)_n$ -substituted heteroaryl; wherein n is 1, 2, or 3 and the substituents for said substituted R^9 groups are each independently selected from the group consisting of: (1) $-OH$; (2) $-CO_2R^{14}$; (3) $-CH_2OR^{14}$, (3) halo, (4) alkyl; (5) amino; (6) trityl; (7) heterocycloalkyl; (8) arylalkyl; (9) heteroaryl and (10) heteroarylalkyl. wherein R^{14} is independently selected from the group consisting of: H and alkyl. In another embodiment, R^9 may be selected from the group consisting of: (1) $-(CH_2)_n$ -imidazolyl; (2) $-(CH_2)_n$ -substituted imidazolyl; (3) $-(CH_2)_n$ -morpholinyl; (4) $-(CH_2)_n$ -substituted morpholinyl, (5) $-(CH_2)_n$ -piperazinyl, and (6) $-(CH_2)_n$ -substituted piperazinyl, wherein n is 1, 2, or 3. R^{11} may be selected from the group consisting of: alkyl, cycloalkyl and substituted cycloalkyl wherein the substituents are selected from the group consisting of: halo, alkyl and amino; and



R^{11a} may be selected from: alkyl, unsubstituted aryl, and substituted aryl, cycloalkyl or substituted cycloalkyl, wherein the substituents on said substituted groups are selected from the group consisting of: halo, $-CN$ or CF_3 ; (3) R^2 , R^2 , and R^{22} are H; and (4) R^{46} is selected from the group consisting of: unsubstituted aryl, 2247 substituted aryl wherein the substituents are selected from the group consisting of: alkyl, alkylcarbonyl and haloalkyl, and wherein R^{44} is selected from the group consisting of: H or $-C(O)NH_2$. In another embodiment, R^8 may be selected from the group consisting of: (1) group 2.0 wherein R^{11} is selected from the group consisting of: t-butyl and cyclohexyl; (2) group 3.0 wherein R^{11} is selected from the group consisting of: methyl and t-butyl; (3) group 4.0 wherein, R^{12} is H, and R^{11a} is selected from the group consisting of: t-butyl, cyanophenyl, chlorophenyl, fluorophenyl and cyclohexyl; (4) group 5.0 wherein R^{21} and R^{22} are H, and R^{46}



is selected from the group consisting of: R^{44} is $-C(O)NH_2$. R^8 may be group 4.0.

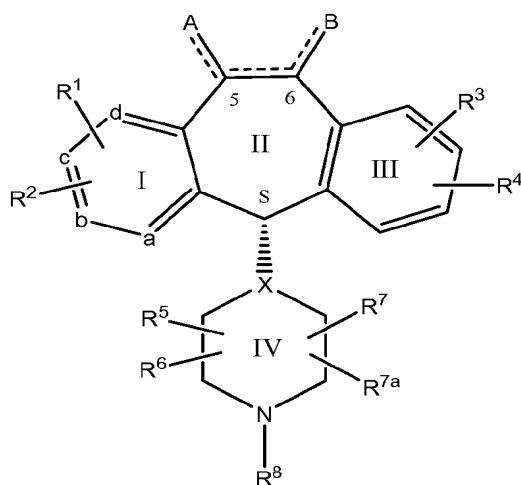
[00160] In one embodiment, the optional bond between C5 and C6 may be present and A is H and B is R⁹.

[00161] In one embodiment, (1) R¹ to R⁴ each may be independently selected from the group consisting of: H and halo; (2) R⁵, R⁶, R⁷, and R^{7a} are H; (3) a is N and the remaining b, c and d substituents are carbon; (4) the optional bond between C5 and C6 is present; (5) A is H; (6) B is R⁹; (7) R⁸ is group 2.0 or 4.0; (8) R¹¹ is selected from the group consisting of: alkyl, cycloalkyl and substituted cycloalkyl wherein the substituents are selected from the group consisting of: halo, alkyl and amino; (9) R^{11a} is selected from the group consisting of: alkyl, unsubstituted aryl, substituted aryl, cycloalkyl or substituted cycloalkyl, wherein the substituents on said substituted groups are selected from the group consisting of: halo, —CN and CF₃; (10) R¹² is H; (11) R⁹ is selected from the group consisting of: (a) —(CH₂)_n-heterocycloalkyl; (b) —(CH₂)_n-substituted heterocycloalkyl; (c) —(CH₂)_n-heteroaryl, and (d) —(CH₂)_n-substituted heteroaryl; wherein n is 1, 2, or 3 and the substituents for said substituted R⁹ groups are each independently selected from the group consisting of: (1) —OH; (2) —CO₂R¹⁴; (3) —CH₂OR¹⁴, (4) halo, (5) alkyl; (6) amino; (7) trityl; (8) heterocycloalkyl; (9) arylalkyl; (10) heteroaryl and (11) heteroarylalkyl; wherein R¹⁴ is independently selected from the group consisting of: H and alkyl; and (12) X is N or CH.

[00162] In another embodiment, (1) R¹ to R⁴ each may be independently selected from H, Br or Cl; (2) R⁹ is selected from the group consisting of: (a) —(CH₂)_n-imidazolyl; (b) —(CH₂)_n-substituted imidazolyl; (c) —(CH₂)_n-morpholinyl; (d) —(CH₂)_n-substituted morpholinyl, (e) —(CH₂)_n-piperazinyl, or (f) —(CH₂)_n-substituted piperazinyl, wherein n is 1, 2, or 3; (3) R¹¹ is selected from the group consisting of: t-butyl and cyclohexyl; (4) R¹² is H; and (5) R^{11a} is selected from the group consisting of: t-butyl, cyanophenyl, chlorophenyl, fluorophenyl and cyclohexy.

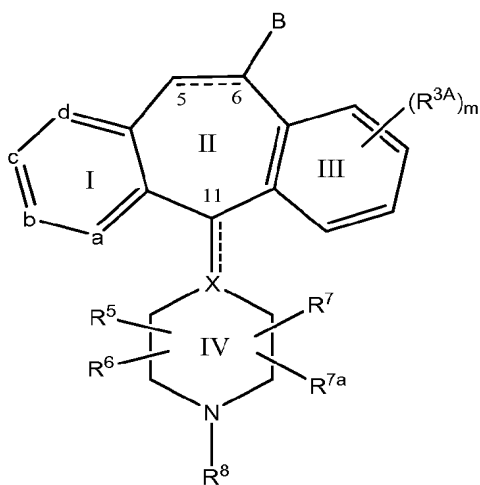
[00163] In yet another embodiment, (1) R¹ and R² are H; (2) R³ is H; (3) R⁴ is Cl; (5) R⁸ is 4.0 wherein R^{11a} is cyanophenyl; and R¹² is H; and (6) R⁹ is selected from the group consisting of: —CH₂-imidazolyl, and —CH₂-imidazolyl wherein said imidazolyl moiety is substituted with a methyl group.

[00164] In one embodiment, the farnesyl transferase inhibitor compound may have the formula:



X may be N.

[00165] In one embodiment, the farnesyl transferase inhibitor compound may have the formula:



wherein:

(A) one of a, b, c and d represents N or N⁺O⁻, and the remaining a, b, c, and d groups represent CR¹ wherein each R¹ group on each carbon is the same or different; or

(B) each a, b, c, and d group represents CR¹ wherein each R¹ group on each carbon is the same or different;

(C) the dotted lines (---) represent optional bonds;

(D) X represents N or CH when the optional bond to C11 is absent, and represents C when the optional bond to C11 is present;

(E) R¹ is selected from the group consisting of: (1) H; (2) halo; (3) —CF₃; (4) —OR¹⁰; (5) COR¹⁰; (6) —SR¹⁰; (7) —S(O)_nR¹⁵; (8) —N(R¹⁰)₂; (9) —NO₂; (10) —OC(O)R¹⁰; (11)

CO_2R^{10} ; (12) $-\text{OCO}_2\text{R}^{10}$; (13) $-\text{CN}$; (14) $-\text{NR}^{10}\text{COOR}^{15}$; (15) $-\text{SR}^{15}\text{C}(\text{O})\text{OR}^{15}$; (16) $-\text{SR}^{15}\text{N}(\text{R}^{13})_2$ wherein each R^{13} is independently selected from the group consisting of: H and $-\text{C}(\text{O})\text{OR}^{15}$, and provided that R^{15} in $-\text{SR}^{15}\text{N}(\text{R}^{13})_2$ is not $-\text{CH}_2$; (17) benzotriazol-1-yloxy; (18) tetrazol-5-ylthio; (19) substituted tetrazol-5-ylthio; (20) alkynyl; (21) alkenyl; (22) alkyl; (23) alkyl substituted with one or more substituents independently selected from the group consisting of: halogen, $-\text{OR}^{10}$ and $-\text{CO}_2\text{R}^{10}$; (24) alkenyl substituted with one or more substituents independently selected from the group consisting of: halogen, $-\text{OR}^{10}$ and $-\text{CO}_2\text{R}^{10}$;

(F) Each R is independently selected from the group consisting of: (1) halo; (2) $-\text{CF}_3$; (3) $-\text{OR}^{10}$; (4) COR^{10} ; (5) $-\text{SR}^{10}$; (6) $-\text{S}(\text{O})_t\text{R}^{15}$; (7) $-\text{N}(\text{R}^{10})_2$; (8) $-\text{NO}_2$; (9) $-\text{OC}(\text{O})\text{R}^{10}$; (10) CO_2R^{10} ; (11) $-\text{OCO}_2\text{R}^{10}$; (12) $-\text{CN}$; (13) $-\text{NR}^{10}\text{COOR}^{15}$; (14) $-\text{SR}^{15}\text{C}(\text{O})\text{OR}^{15}$; (15) $-\text{SR}^{15}\text{N}(\text{R}^{13})_2$ wherein each R^{13} is independently selected from the group consisting of: H and $-\text{C}(\text{O})\text{OR}^{15}$, and provided that R^{15} in $-\text{SR}^{15}\text{N}(\text{R}^{13})_2$ is not $-\text{CH}_2$; (16) benzotriazol-1-yloxy; (17) tetrazol-5-ylthio; (18) substituted tetrazol-5-ylthio; (19) alkynyl; (20) alkenyl; (21) alkyl; (22) alkyl substituted with one or more substituents independently selected from the group consisting of: halogen, $-\text{OR}^{10}$ and $-\text{CO}_2\text{R}^{10}$; and (23) alkenyl substituted with one or more substituents independently selected from the group consisting of: halogen, $-\text{OR}^{10}$ and $-\text{CO}_2\text{R}^{10}$;

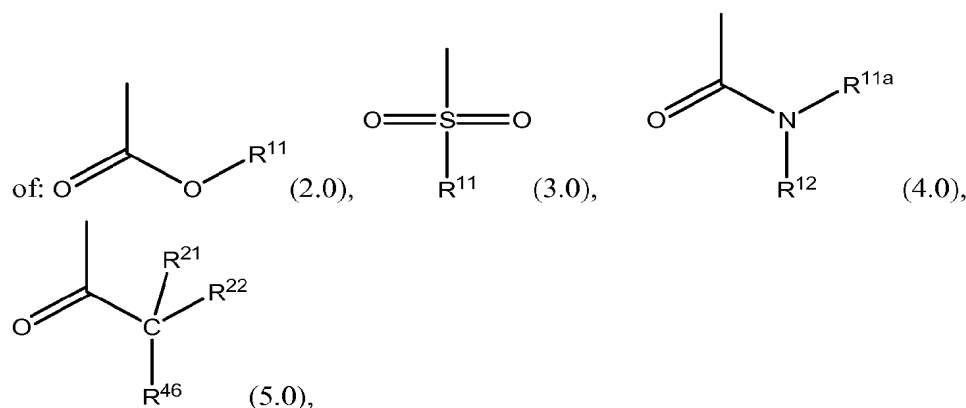
(G) m is 0, 1 or 2;

(H) t is 0, 1 or 2

(I) R^5 , R^6 , R^7 and R^{7a} are each independently selected from the group consisting of: (1) H; (2) $-\text{CF}_3$; (3) $-\text{COR}^{10}$; (4) alkyl; (5) unsubstituted aryl; (6) alkyl substituted with one or more groups selected from the group consisting of: $-\text{OR}^{10}$, $-\text{SR}^{10}$, $-\text{S}(\text{O})_t\text{R}^{15}$, $-\text{NR}^{10}\text{COOR}^{15}$, $-\text{N}(\text{R}^{10})_2$, $-\text{NO}_2$, $-\text{C}(\text{O})\text{R}^{10}$; $-\text{OCOR}^{10}$, $-\text{OCO}_2\text{R}^{15}$, CO_2R^{10} , and $\text{OPO}_3\text{R}^{10}$; and (7) aryl substituted with one or more groups selected from the group consisting of: $-\text{OR}^{10}$, $-\text{SR}^{10}$, $-\text{S}(\text{O})_t\text{R}^{15}$, $-\text{NR}^{10}\text{COOR}^{15}$, $-\text{N}(\text{R}^{10})_2$, $-\text{NO}_2$, $-\text{C}(\text{O})\text{R}^{10}$; $-\text{OCOR}^{10}$, $-\text{OCO}_2\text{R}^{15}$, $-\text{CO}_2\text{R}^{10}$, and $\text{OPO}_3\text{R}^{10}$; or

(J) R^5 together with R^6 represents $=\text{O}$ or $=\text{S}$;

(K) R^8 is selected from the group consisting



(L) R^{10} is selected from the group consisting of: H; alkyl; aryl and arylalkyl;

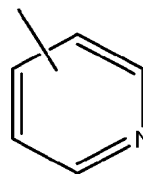
(M) R^{11} is selected from: (1) alkyl; (2) substituted alkyl; (3) unsubstituted aryl; (4) substituted aryl; (5) unsubstituted cycloalkyl; (6) substituted cycloalkyl; (7) unsubstituted heteroaryl; (8) substituted heteroaryl; (9) heterocycloalkyl; and (10) substituted heterocycloalkyl; wherein said substituted alkyl, substituted cycloalkyl, and substituted heterocycloalkyl R^{11} groups are substituted with one or more substituents selected from the group consisting of: (1) —OH; (2) fluoro; and (3) alkyl; and wherein said substituted aryl and substituted heteroaryl R^{11} groups are substituted with one or more substituents selected from the group consisting of: (1) —OH; (2) halogen; and (3) alkyl;

(N) R^{11a} is selected from the group consisting of: (1) H; (2) OH; (3) alkyl; (4) substituted alkyl; (5) unsubstituted aryl; (6) substituted aryl; (7) unsubstituted cycloalkyl; (8) substituted cycloalkyl; (9) unsubstituted heteroaryl; (10) substituted heteroaryl; (11) heterocycloalkyl; and (12) substituted heterocycloalkyl; wherein said substituted alkyl, substituted cycloalkyl, and substituted heterocycloalkyl R^{11a} groups are substituted with one or more substituents selected from the group consisting of: (1) —OH; (2) —CN; (3) —CF₃; (4) fluoro; (5) alkyl; (6) cycloalkyl; (7) heterocycloalkyl; (8) arylalkyl; (9) heteroarylalkyl; (10) alkenyl and (11) heteroalkenyl; and wherein said substituted aryl and substituted heteroaryl R^{11a} groups are substituted with one or more substituents selected from the group consisting of: (1) —OH; (2) —CN; (3) —CF₃; (4) halogen; (5) alkyl; (6) cycloalkyl; (7) heterocycloalkyl; (8) arylalkyl; (9) heteroarylalkyl; (10) alkenyl and (11) heteroalkenyl; (O) R^{12} is selected from the group consisting of: H, alkyl, piperidine Ring V, cycloalkyl, and -alkyl-(piperidine Ring V);

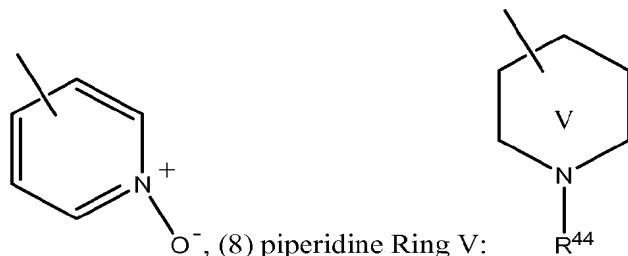
(P) R^{15} is selected from the group consisting of: alkyl and aryl;

(Q) R^{21} , R^{22} and R^{46} are independently selected from the group consisting of: (1) H; (2) alkyl; (3) unsubstituted aryl; (4) substituted aryl substituted with one or more substituents

selected from the group consisting of: alkyl, halogen, CF_3 or OH; (5) unsubstituted cycloalkyl; (6) substituted cycloalkyl substituted with one or more substituents selected from



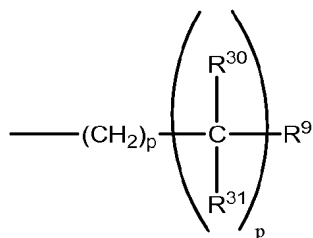
the group consisting of: alkyl, halogen, CF_3 or OH; (7) heteroaryl of the formula,



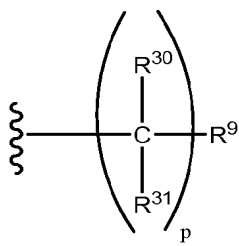
, O^- , (8) piperidine Ring V: R^{44} wherein R^{44} is selected from the group consisting of: (a) H, (b) alkyl; (c) alkylcarbonyl; (d) alkyloxy carbonyl; (e) haloalkyl and (f) $-\text{C}(\text{O})\text{NH}(\text{R}^{51})$;

(R) R^{51} is selected from the group consisting of: $-\text{H}$ and alkyl (e.g., methyl, ethyl, propyl, butyl and t-butyl);

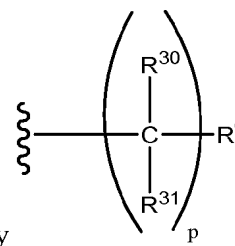
(S) B is the group:



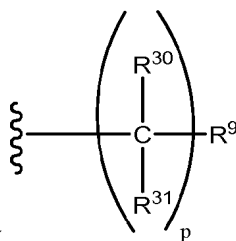
(T) in said B group: (1) p of the $-(\text{CH}_2)_p-$ moiety is 0; (2) p of the



moiety is 1 to 3; (3) when p is one for the moiety



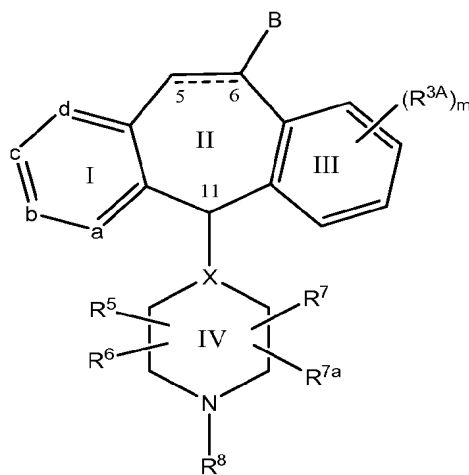
then R^{30} is selected from the group consisting of: $-\text{OH}$ and $-\text{NH}_2$, and R^{31} is alkyl; (4)



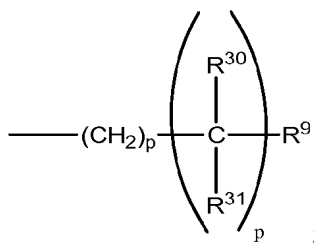
when p is 2 or 3 for the moiety then: (1) for one $\text{—CR}^{30}\text{R}^{31}\text{—}$ moiety, R^{30} is selected from the group consisting of: —OH and —NH_2 , and R^{31} is alkyl; and (2) for the remaining $\text{—CR}^{30}\text{R}^{31}\text{—}$ moieties R^{30} and R^{31} are hydrogen; and (5) R^9 is unsubstituted heteroaryl or substituted heteroaryl, provided that when said heteroaryl group contains nitrogen in the ring, then said heteroaryl group is not bound by a ring nitrogen to the adjacent $\text{—CR}^{30}\text{R}^{31}\text{—}$ moiety when R^{30} is —OH or —NH_2 .

[00166] In one embodiment, (4) a is N; (5) b , c and d are CR^1 groups wherein all of said R^1 substituents are H, or one R^1 substituent is halo and the remaining two R^1 substituents are hydrogen; (6) m is 1, and R^{3A} is halo, or m is 2 and each R^{3A} is the same or different halo (e.g., Br or Cl); and (7) R^5 , R^6 , R^7 , and R^{7a} are H.

[00167] In one embodiment, the farnesyl transferase inhibitor compound may have the formula:

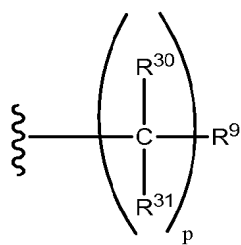


wherein:



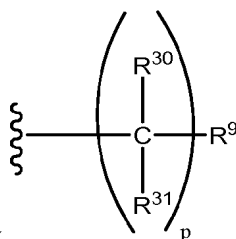
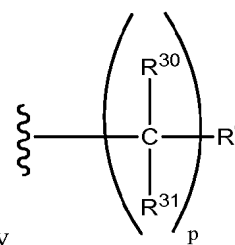
(A) B is the group:

(B) in said B group: (1) p of the $-(CH_2)_p-$ moiety is 0; (2) p of the



moiety is 1 to 3; (3) when p is one for the moiety

then R^{30} is selected from the group consisting of: $-OH$ and $-NH_2$, and R^{31} is alkyl; (d)



when p is 2 or 3 for the moiety

then: (1) for one $-CR^{30}R^{31}-$ moiety,

R^{30} is selected from the group consisting of: $-OH$ and $-NH_2$, and R^{31} is alkyl; and (2) for

the remaining $-CR^{30}R^{31}-$ moieties R^{30} and R^{31} are hydrogen; and (e) R^9 is unsubstituted

heteroaryl or substituted heteroaryl, provided that when said heteroaryl group contains

nitrogen in the ring, then said heteroaryl group is not bound by a ring nitrogen to the adjacent $-CR^{30}R^{31}-$ moiety when R^{30} is $-OH$ or $-NH_2$;

(C) a is N;

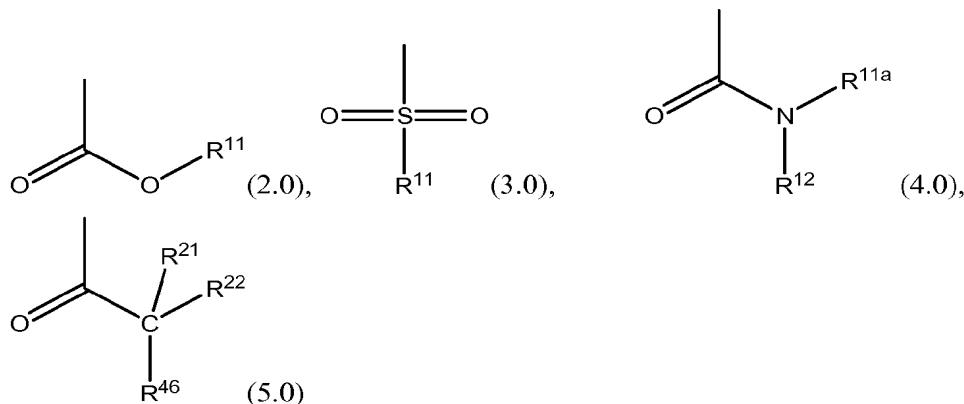
(D) b, c and d are CR^1 groups wherein all of said R^1 substituents are H, or one R^1 substituent is halo and the remaining two R^1 substituents are hydrogen;

(E) m is 1, and R^{3A} is halo, or m is 2 and each R^{3A} is the same or different halo;

(F) X is N or CH;

(G) R^5 , R^6 , R^7 , and R^{7a} are H;

(H) R^8 is selected from the group consisting of:



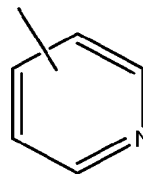
(I) R^{11} is selected from: (1) alkyl; (2) substituted alkyl; (3) unsubstituted aryl; (4) substituted aryl; (5) unsubstituted cycloalkyl; (6) substituted cycloalkyl; (7) unsubstituted heteroaryl; (8) substituted heteroaryl; (9) heterocycloalkyl; and (10) substituted heterocycloalkyl; wherein said substituted alkyl, substituted cycloalkyl, and substituted heterocycloalkyl R^{11} groups are substituted with one or more substituents selected from the group consisting of: (1) —OH; (2) fluoro; and (3) alkyl; and wherein said substituted aryl and substituted heteroaryl R^{11} groups are substituted with one or more substituents selected from the group consisting of: (1) —OH; (2) halogen; and (3) alkyl;

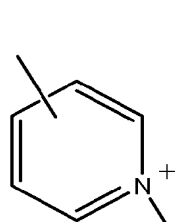
(J) R^{11a} is selected from the group consisting of: (1) H; (2) OH; (3) alkyl; (4) substituted alkyl; (5) unsubstituted aryl; (6) substituted aryl; (7) unsubstituted cycloalkyl; (8) substituted cycloalkyl; (9) unsubstituted heteroaryl; (10) substituted heteroaryl; (11) heterocycloalkyl; and (12) substituted heterocycloalkyl; wherein said substituted alkyl, substituted cycloalkyl, and substituted heterocycloalkyl R^{11a} groups are substituted with one or more substituents selected from the group consisting of: (1) —OH; (2) —CN; (3) —CF₃; (4) fluoro; (5) alkyl; (6) cycloalkyl; (7) heterocycloalkyl; (8) arylalkyl; (9) heteroarylalkyl; (10) alkenyl and (11) heteroalkenyl; and wherein said substituted aryl and substituted heteroaryl R^{11a} groups are substituted with one or more substituents selected from the group consisting of: (1) —OH; (2) —CN; (3) —CF₃; (4) halogen; (5) alkyl; (6) cycloalkyl; (7) heterocycloalkyl; (8) arylalkyl; (9) heteroarylalkyl; (10) alkenyl and (11) heteroalkenyl;

(K) R^{12} is selected from the group consisting of: H, alkyl, piperidine Ring V, cycloalkyl, and -alkyl-(piperidine Ring V);

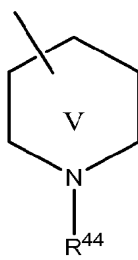
(L) R^{21} , R^{22} and R^{46} are independently selected from the group consisting of: (1) H; (2) alkyl; (3) unsubstituted aryl; (4) substituted aryl substituted with one or more substituents selected from the group consisting of: alkyl, halogen, CF₃ or OH; (5) unsubstituted cycloalkyl; (6) substituted cycloalkyl substituted with one or more substituents selected from

the group consisting of: alkyl, halogen, CF₃ or OH; (7) heteroaryl of the formula,





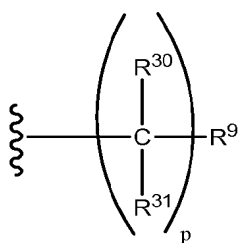
, (8) piperidine Ring V:



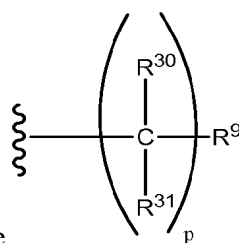
wherein R^{44} is selected from the group consisting of: (a) H, (b) alkyl; (c) alkylcarbonyl; (d) alkyloxy carbonyl; (e) haloalkyl and (f) $—C(O)NH(R^{51})$; and

(M) R^{51} is selected from the group consisting of: H and alkyl (e.g., methyl, ethyl, propyl, butyl and t-butyl).

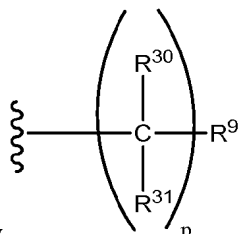
[00168] In one embodiment, (A) in the B group: (1) p of the



moiety is 0; (2) p of the

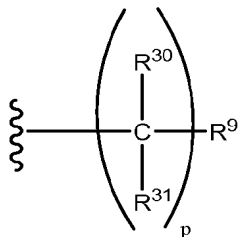


moiety is 1 to 2; (3) when p



is one for the moiety

then R^{30} is selected from the group consisting of: $—OH$ and $—NH_2$, and R^{31} is C_1 - C_2 alkyl; (4) when p is 2 or 3 for the moiety



then: (1) for one $—CR^{30}R^{31}—$ moiety, R^{30} is selected from the group consisting of: $—OH$ and $—NH_2$, and R^{31} is C_1 - C_2 alkyl; and (2) for the remaining $—CR^{30}R^{31}—$ moieties R^{30} and R^{31} are hydrogen; and (5) R^9 is imidazolyl or substituted imidazolyl, provided that said imidazolyl group is not bound by a ring nitrogen to the adjacent $—CR^{30}R^{31}—$ moiety when R^{30} is $—OH$ or $—NH_2$;

(B) R^8 is 2.0;

(C) R^{11} is alkyl;

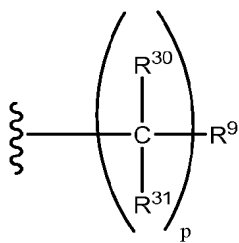
(D) X is N;

(E) b, c and d are CR¹ groups wherein all of said R¹ substituents are H;

(F) m is 1, and R^{3A} is halo; and

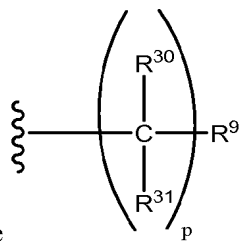
(G) X is N.

In one embodiment, in the B group: (1) p of the —(CH₂)_p— moiety is 0; (2) p of the



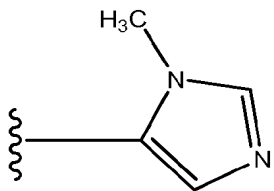
moiety is 1; (3) R³⁰ is selected from the group consisting of: —OH and —NH₂, and R³¹ is C₁-C₂ alkyl; and (4) R⁹ is substituted imidazolyl wherein said the substituent is an alkyl group, provided that said imidazolyl group is not bound by a ring nitrogen to the adjacent —CR³⁰R³¹— moiety.

[00169] In another embodiment, (A) in said B group: (1) p of the —(CH₂)_p— moiety is 0;



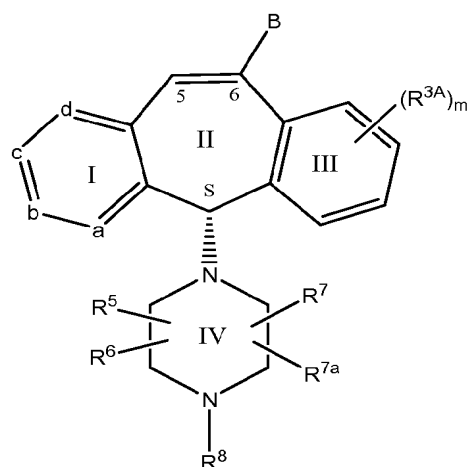
(2) p of the moiety is 1; (3) R³⁰ is —OH, and R³¹ is methyl; and (4) R⁹ is substituted imidazolyl wherein the substituent is a methyl group, provided that said imidazolyl group is not bound by a ring nitrogen to the adjacent —CR³⁰R³¹— moiety; and (B) R^{3A} is Cl; and (C) R¹¹ is alkyl.

R⁹ may be



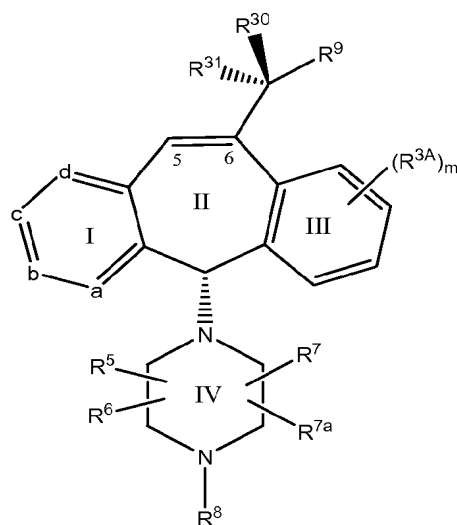
R¹¹ may be t-butyl.

[00170] In one embodiment, the farnesyl transferase inhibitor compound may have the formula:



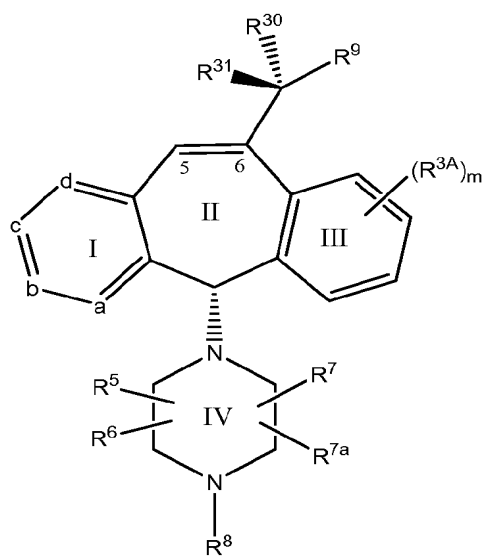
wherein all substituents may be as defined above.

[00171] In one embodiment, the farnesyl transferase inhibitor compound may have the formula:



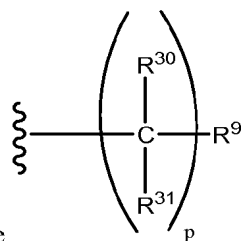
wherein all substituents may be as defined above.

[00172] In one embodiment, the farnesyl transferase inhibitor compound may have the formula:



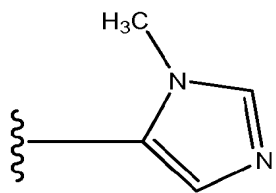
wherein all substituents may be as defined above.

[00173] In one embodiment, (A) in the B group: (1) p of the $-(CH_2)_p-$ moiety is 0; (2) p



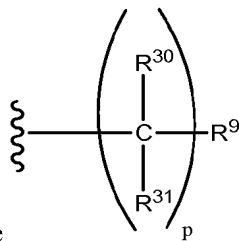
of the moiety is 1; (3) R^{30} is $-OH$, and R^{31} is methyl; and (4) R^9 is substituted imidazolyl wherein the substituent is a methyl group, provided that said imidazolyl group is not bound by a ring nitrogen to the adjacent $-CR^{30}R^{31}-$ moiety; and (B) R^{3A} is Cl; and (C) R^{11} is alkyl.

R^9 may be



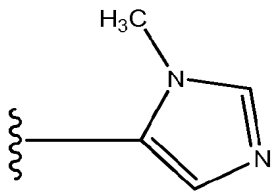
R^{11} may be t-butyl.

[00174] In one embodiment, (A) in the B group: (1) p of the $-(CH_2)_p-$ moiety is 0; (2) p



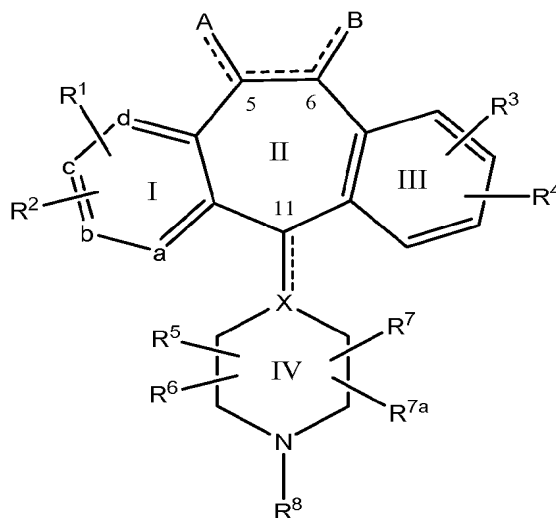
of the moiety is 1; (3) R^{30} is $-OH$, and R^{31} is methyl; and (4) R^9 is substituted imidazolyl wherein the substituent is a methyl group, provided that said imidazolyl group is not bound by a ring nitrogen to the adjacent $-CR^{30}R^{31}-$ moiety; and (B) R^{3A} is Cl; and (C) R^{11} is alkyl.

R^9 may be



R^{11} may be t-butyl.

[00175] In certain embodiments, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

wherein:

one of a, b, c and d represents N or N⁺O⁻, and the remaining a, b, c, and d groups represent carbon, wherein each carbon has an R¹ or R² group bound to said carbon; or

each of a, b, c, and d is carbon, wherein each carbon has an R¹ or R² group bound to said carbon;

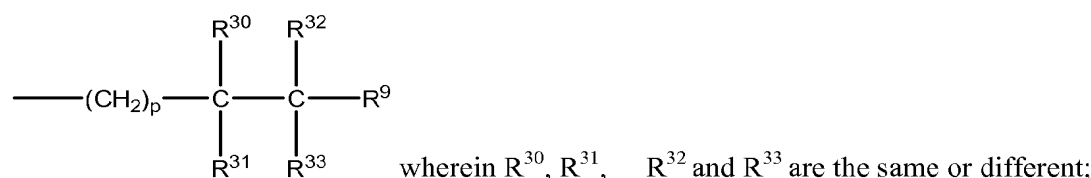
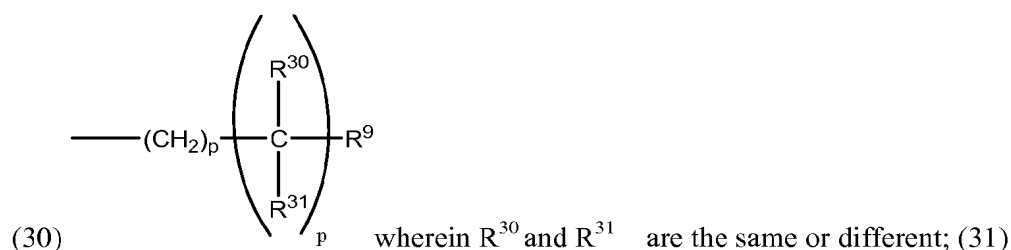
the dotted lines (—) represent optional bonds;

X represents N or CH when the optional bond is absent, and represents C when the optional bond is present;

when the optional bond is present between carbon atom 5 and carbon atom 6 then there is only one A substituent bound to carbon atom 5 and there is only one B substituent bound to carbon atom 6 and A or B is other than H;

when the optional bond is not present between carbon atom 5 and carbon atom 6, then there are two A substituents bound to carbon atom 5 and two B substituents bound to carbon atom 6, wherein each A and B substituent is independently selected from the group consisting of:

(1) —H; (2) —R⁹; (3) —R⁹—C(O)—R⁹; (4) —R⁹—CO₂—R^{9a}; (5) —(CH₂)_pR²⁶; (6) —C(O)N(R⁹)₂, wherein each R⁹ is the same or different; (7) —C(O)NHR⁹; (8) —C(O)NH—CH₂—C(O)—NH₂; (9) —C(O)NHR²⁶; (10) —(CH₂)_pC(R⁹)—O—R^{9a}; (11) —(CH₂)_p(R⁹)₂, wherein each R⁹ is the same or different; (12) —(CH₂)_pC(O)R⁹; (13) —(CH₂)_pC(O)R^{27a}; (14) —(CH₂)_pC(O)N(R⁹)₂, wherein each R⁹ is the same or different; (15) —(CH₂)_pC(O)NH(R⁹); (16) —(CH₂)_pC(O)N(R²⁶)₂, wherein each R²⁶ is the same or different; (17) —(CH₂)_pN(R⁹)—R^{9a}; (18) —(CH₂)_pN(R²⁶)₂, wherein R²⁶ is the same or different; (19) —(CH₂)_pNHC(O)R⁵⁰; (20) —(CH₂)_pNHC(O)₂R⁵⁰; (21) —(CH₂)_pN(C(O)R^{27a})₂ wherein each R^{27a} is the same or different; (22) —(CH₂)_pNR⁵¹C(O)R²⁷, or R⁵¹ and R²⁷ taken together with the atoms to which they are bound form a heterocycloalkyl ring consisting of, 5 or 6 members, provided that when R⁵¹ and R²⁷ form a ring, R⁵¹ is not H; (23) —(CH₂)_pNR⁵¹C(O)NR²⁷, or R⁵¹ and R²⁷ taken together with the atoms to which they are bound form a heterocycloalkyl ring consisting of 5 or 6 members, provided that when R⁵¹ and R²⁷ form a ring, R⁵¹ is not H; (24) —(CH₂)_pNR⁵¹C(O)N(R^{27a})₂, wherein each R^{27a} is the same or different; (25) —(CH₂)_pNHSO₂N(R⁵¹)₂, wherein each R⁵¹ is the same or different; (26) —(CH₂)_pNHCO₂R⁵⁰; (27) —(CH₂)_pNC(O)NHR⁵¹; (28) —(CH₂)_pCO₂R⁵¹; (29) —NHR⁹;



(32) -alkenyl-CO₂R^{9a}; (33) -alkenyl- C(O)R^{9a}; (34) -alkenyl-CO₂R⁵¹; (35) -alkenyl-C(O)—R^{27a}; (36) (CH₂)_p-alkenyl- CO₂—R⁵¹; (37) —(CH₂)_pC=NOR⁵¹ and (38) —(CH₂)_p-Phthalimid;

p is 0, 1, 2, 3 or 4;

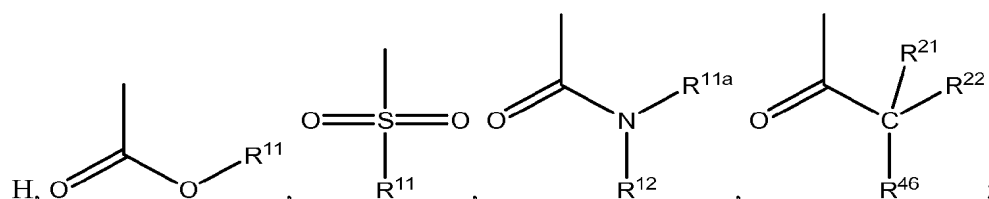
each R¹ and R² is independently selected from H, Halogen, —CF₃, —OR¹⁰, COR¹⁰, —

SR¹⁰, —S(O)_tR¹⁵ wherein t is 0, 1 or 2, —N(R¹⁰)₂, —NO₂, —OC(O)R¹⁰, CO₂R¹⁰, —OCO₂R¹⁵, —CN, —NR¹⁰COOR¹⁵, —SR¹⁵C(O)OR¹⁵ —SR¹⁵N(R¹³)₂ provided that R¹⁵ in —SR¹⁵N(R¹³)₂ is not —CH₂, and wherein each R¹³ is independently selected from H or —C(O)OR¹⁵, benzotriazol-1-yloxy, tetrazol-5-ylthio, or substituted tetrazol-5-ylthio, alkynyl, alkenyl or alkyl, said alkyl or alkenyl group optionally being substituted with halogen, —OR¹⁰ or —CO₂R¹⁰;

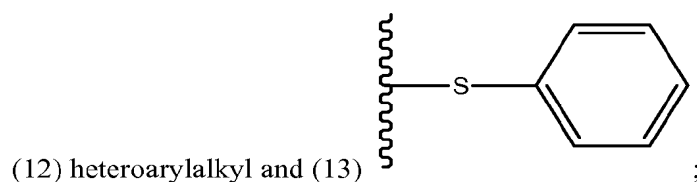
R³ and R⁴ are the same or different and each independently represent H, or any of the substituents of R¹ and R²;

R⁵, R⁶, R⁷ and R^{7a} each independently represent H, —CF₃, —COR¹⁰, alkyl or aryl, said alkyl or aryl optionally being substituted with —OR¹⁰, —SR¹⁰, —S(O)_tR¹⁵, —NR¹⁰COOR¹⁵, —N(R¹⁰)₂, —NO₂, —C(O)R¹⁰, —OCOR¹⁰, —OCO₂R¹⁵, —CO₂R¹⁰, OPO₃R¹⁰, or R⁵ is combined with R⁶ to represent =O or =S;

R⁸ is selected from the group consisting of:



R^9 is selected from the group consisting of: (1) heteroaryl; (2) substituted heteroaryl; (3) arylalkoxy; (4) substituted arylalkoxy; (5) heterocycloalkyl; (6) substituted heterocycloalkyl; (7) heterocycloalkylalkyl; (8) substituted heterocycloalkylalkyl; (9) heteroarylalkyl; (10) substituted heteroarylalkyl; (11) heteroarylalkenyl; (12) substituted heteroarylalkenyl; (13) heteroarylalkynyl; (14) substituted heteroarylalkynyl; (15) arylalkyl; (16) substituted arylalkyl; (17) alkenyl, and (18) substituted alkenyl; wherein said substituted R^9 groups are substituted with one or more substituents selected from the group consisting of: (1) $-\text{OH}$; (2) $-\text{CO}_2R^{14}$; (3) $-\text{CH}_2\text{OR}^{14}$; (4) halogen; (5) alkyl; (6) amino; (7) trityl; (8) heterocycloalkyl; (9) cycloalkyl; (10) arylalkyl; (11) heteroaryl;



wherein

R^{14} is independently selected from the group consisting of: H; alkyl; aryl, arylalkyl, heteroaryl and heteroarylalkyl;

R^{9a} is selected from the group consisting of: alky and arylalkyl;

R^{10} is selected from the group consisting of: H; alkyl; aryl and arylalkyl;

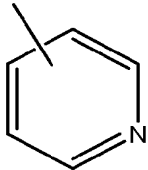
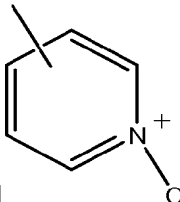
R^{11} is selected from the group consisting of: (1) alkyl; (2) substituted alkyl; (3) aryl; (4) substituted aryl; (5) cycloalkyl; (6) substituted cycloalkyl; (7) heteroaryl; (8) substituted heteroaryl; (9) heterocycloalkyl; and (10) substituted heterocycloalkyl; wherein said substituted R^{11} groups have 1, 2 or 3 substituents selected from the group consisting of: (1) $-\text{OH}$; (2) halogen and (3) alkyl;

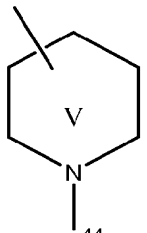
R^{11a} is selected from the group consisting of: (1) H; (2) OH; (3) alkyl; (4) substituted alkyl; (5) aryl; (6) substituted aryl; (7) cycloalkyl; (8) substituted cycloalkyl; (9) heteroaryl; (10) substituted heteroaryl; (11) heterocycloalkyl; and (12) substituted heterocycloalkyl; wherein said substituted R^{11a} groups have one or more substituents selected from the group consisting of: (1) $-\text{OH}$; (2) $-\text{CN}$; (3) $-\text{CF}_3$; (4) halogen; (5) alkyl; (6) cycloalkyl; (7) heterocycloalkyl, (8) arylalkyl; (9) heteroarylalkyl; (10) alkenyl and (11) heteroalkenyl;

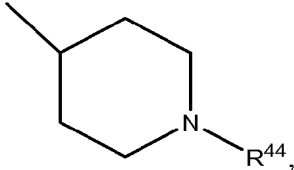
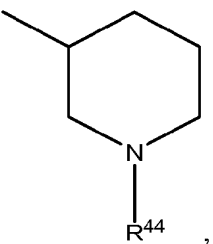
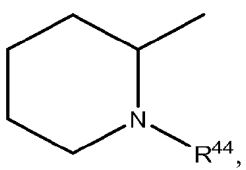
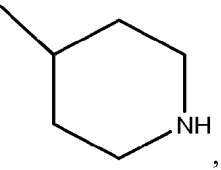
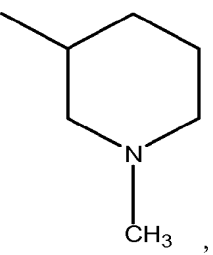
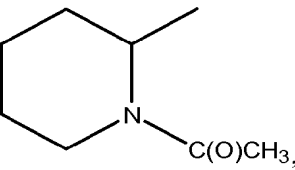
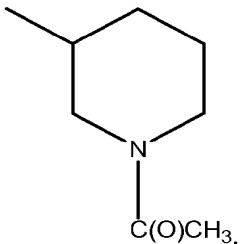
R^{12} is selected from the group consisting of: H, and alkyl;

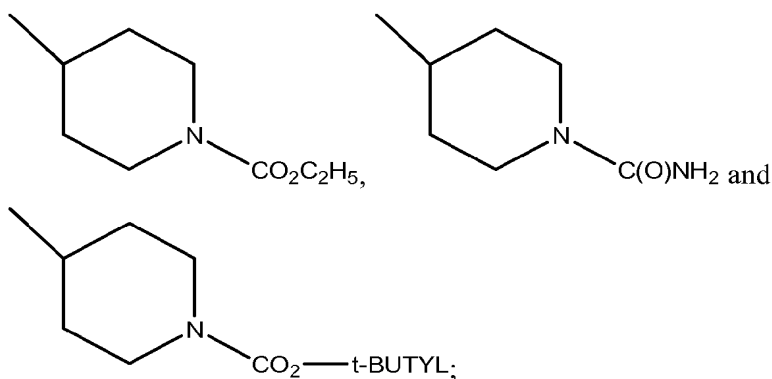
R^{15} is selected from the group consisting of: alkyl and aryl;

R^{21} , R^{22} and R^{46} are independently selected from the group consisting of: (1) —H; (2) alkyl; (3) aryl; (4) substituted aryl, optionally substituted with one or more substituents selected from the group consisting of: alkyl, halogen, CF_3 and OH; (5) cycloalkyl; (6) substituted cycloalkyl; optionally substituted with one or more substituents selected from the group consisting of: alkyl, halogen, CF_3 and OH; (7)

heteroaryl of the formula,  and ⁺ O[−]; and (8) heterocycloalkyl

of the formula:  wherein R^{44} is selected from the group consisting of: (1) —H; (2) alkyl; (3) alkylcarbonyl; (4) alkyloxy carbonyl; (5) haloalkyl and (6) —C(O)NH(R^{51}); when R^{21} , R^{22} or R^{46} is the heterocycloalkyl of the formula above, Ring V is

selected from the group consisting of: , , , , , , and .



R^{26} is selected from the group consisting of: (1) ---H ; (2) alkyl; (3) alkoxy; (4) $\text{---CH}_2\text{---CN}$; (5) R^9 ; (6) $\text{---CH}_2\text{CO}_2\text{H}$; (7) $\text{---C}(\text{O})\text{alkyl}$ and (8) $\text{CH}_2\text{CO}_2\text{alkyl}$;

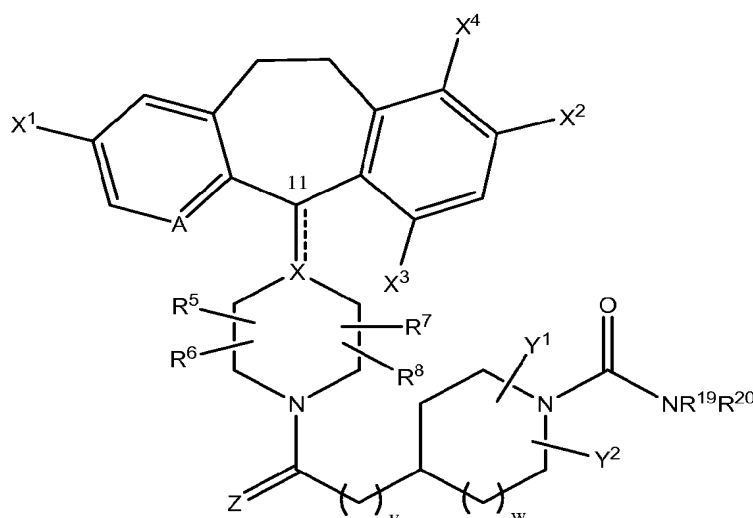
R^{27} is selected from the group consisting of: (1) ---H ; (2) ---OH ; (3) alkyl and (4) alkoxy; R^{27a} is selected from the group consisting of: (1) alkyl and (2) alkoxy;

R^{30} through R^{33} are independently selected from the group consisting of: (1) ---H ; (2) ---OH ; (3) =O ; (4) alkyl; (5) aryl and (6) arylalkyl;

R^{50} is selected from the group consisting of: (1) alkyl; (2) heteroaryl; (3) substituted heteroaryl and (4) amino; wherein said substituents on said substituted R^{50} groups are independently selected from the group consisting of: alkyl; halogen; and ---OH ;

R^{50a} is selected from the group consisting of: (1) heteroaryl; (2) substituted heteroaryl and (3) amino; R^{51} is selected from the group consisting of: ---H , and alkyl.

[00176] In another aspect, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount, wherein:

A represents N or N-oxide;

X represents N, CH or C, such that when X is N or CH, there is a single bond to carbon atom 11 as represented by the solid line; or when X is C, there is a double bond to carbon atom 11, as represented by the solid and dotted lines;

X¹ and X² are independently selected from bromo or chloro, and X³ and X⁴ are independently selected from hydrogen, bromo or chloro provided that at least one of X³ and X⁴ is hydrogen;

Y¹ and Y² are independently selected from hydrogen or alkyl;

Z is =O or =S;

R⁵, R⁶, R⁷ and R⁸ each independently represents hydrogen, --CF₃, --COR¹⁰, alkyl or aryl, and further wherein R⁵ may be combined with R⁶ to represent =O or =S and/or R⁷ may be combined with R⁸ to represent =O or =S;

R¹⁰, R¹⁹ and R²⁰ independently represent hydrogen, alkyl, alkoxy, aryl, aralkyl, heteroaryl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl and heterocycloalkylalkyl, with the proviso that R¹⁹ and R²⁰ are not both hydrogen;

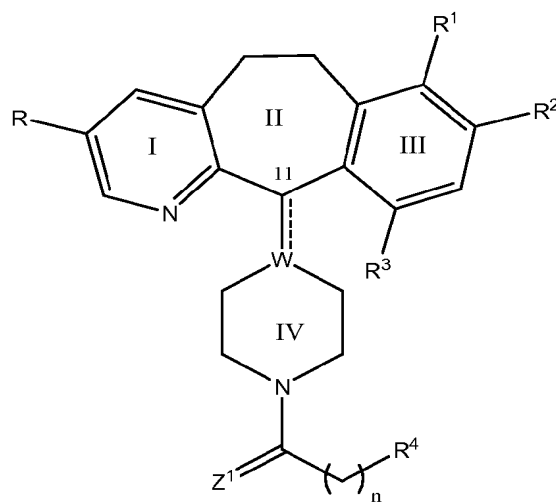
v is zero, 1, 2 or 3; and

w is zero or 1.

[00177] In one embodiment, there may be a single bond at carbon atom 11, X is CH, Z is =O and R⁵, R⁶, R⁷ and R⁸ are hydrogen. In one embodiment, X¹ is bromo, X² is chloro, X³ is

bromo and X^4 is hydrogen. In one embodiment, Z is =O; v is 1, w is 1, and Y^1 and Y^2 are hydrogen. In one embodiment, R^{19} and R^{20} are independently selected from hydrogen, aryl and heterocycloalkyl with the proviso that R^{19} and R^{20} are not both hydrogen. In one embodiment, the aryl group is substituted with alkoxy; and the heterocycloalkyl group is substituted with $-\text{COOR}^{10}$ wherein R^{10} is hydrogen or alkyl. In one embodiment, there is a single bond at carbon atom 11, X is CH, Z is =O, R^5 , R^6 , R^7 and R^8 are hydrogen, X^1 is bromo, X^2 is chloro, X^3 is bromo and X^4 is hydrogen, v is 1, w is 1, and Y^1 and Y^2 are hydrogen, R^{19} and R^{20} are independently selected from hydrogen, aryl and heterocycloalkyl; wherein the aryl group is substituted with alkoxy; and the heterocycloalkyl group is substituted with $-\text{COOR}^{10}$ wherein R^{10} is hydrogen or alkyl, with the proviso that R^{19} and R^{20} are not both hydrogen. In one embodiment, the compound may be any of the compounds shown in Figure 8. In another embodiment, the compound may be any of the compounds shown in Figure 9. In one embodiment, there is a single bond at carbon atom 11, X is CH, Z is =O and R^5 , R^6 , R^7 and R^8 are hydrogen. In one embodiment, X^1 is bromo, X^2 is chloro, X^3 is bromo and X^4 is hydrogen. In one embodiment, Z is =O; v is 1, w is 1, and Y^1 and Y^2 are hydrogen. In one embodiment, R^{19} and R^{20} are independently selected from hydrogen, alkyl, aryl and heterocycloalkyl with the proviso that R^{19} and R^{20} are not both hydrogen. In one embodiment, the alkyl group is substituted with $-\text{OR}^{10}$, alkoxy, $-\text{OCOR}^{10}$, $-\text{CONR}^{10}\text{R}^{12}$ or $-\text{COOR}^{10}$, wherein R^{10} and R^{12} are independently selected from hydrogen, alkyl or alkoxy; the aryl group is substituted with alkoxy; and the heterocycloalkyl group is substituted with $-\text{COOR}^{10}$ wherein R^{10} is hydrogen or alkyl. In one embodiment, there is a single bond at carbon atom 11, X is CH, Z is =O, R^5 , R^6 , R^7 and R^8 are hydrogen, X^1 is bromo, X^2 is chloro, X^3 is bromo and X^4 is hydrogen, v is 1, w is 1, and Y^1 and Y^2 are hydrogen, R^{19} and R^{20} are independently selected from hydrogen, alkyl, aryl and heterocycloalkyl, wherein the alkyl group is substituted with $-\text{OR}^{10}$, alkoxy, $-\text{OCOR}^{10}$, $-\text{CONR}^{10}\text{R}^{12}$ or $-\text{COOR}^{10}$, wherein R^{10} and R^{12} are independently selected from hydrogen, alkyl or alkoxy; the aryl group is substituted with alkoxy; the heterocycloalkyl group is substituted with $-\text{COOR}^{10}$ wherein R^{10} is hydrogen or alkyl, with the proviso that R^{19} and R^{20} are not both hydrogen.

[00178] In another aspect, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

wherein:

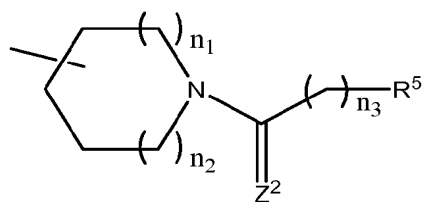
R and R² are independently selected from halo;

R¹ and R³ are independently selected from the group consisting of H and halo,

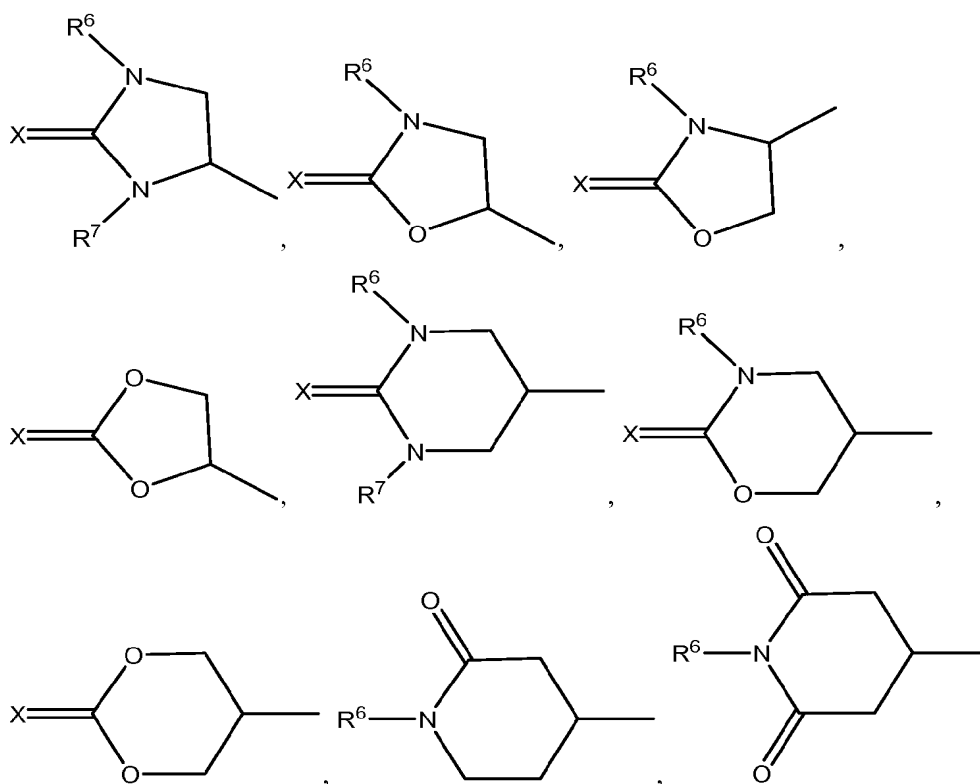
provided that at least one of R¹ and R³ is H;

W is N, CH or C, when the double bond is present at the C-11 position;

R⁴ is



or R⁵; R⁵ is



R⁶ and R⁷ are independently selected from the group consisting of H, alkyl, substituted alkyl, acyl, aryl, aralkyl, heterocycloalkyl and heteroaryl;

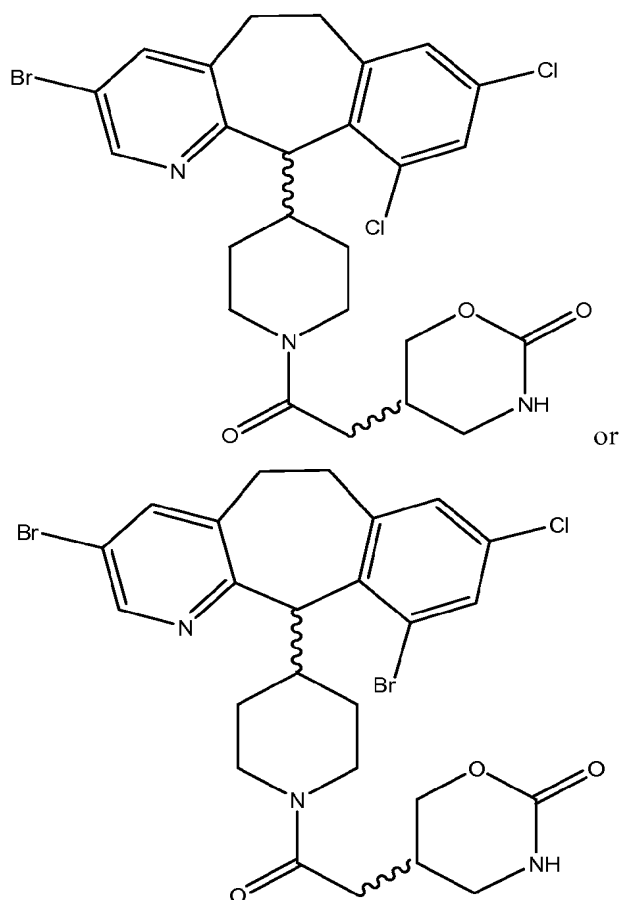
X is =O or =S;

Z¹ and Z² are independently =O or =S;

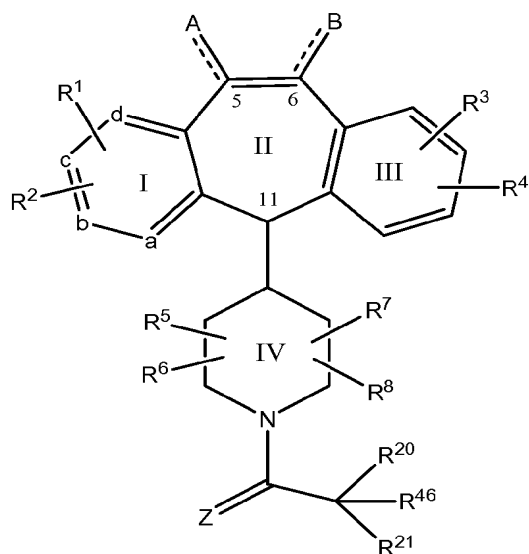
n and n₃ are independently 0, 1 or 2; and

n₁ and n₂ are independently 0 or 1.

[00179] In one embodiment, X is =O and R⁶ and R⁷ are each hydrogen. In one embodiment, n is 1 and n₃ is 0 or 1. In one embodiment, R is bromo and R² is chloro or bromo. In one embodiment, R is bromo, R² is chloro or bromo, R¹ is H, and R³ is chloro or bromo. In one embodiment, R is bromo, R² is chloro or bromo, R³ is H, and R¹ is chloro or bromo. In one embodiment, the compound may any one of the following:



[00180] In another aspect, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

wherein:

a represents N and the remaining b, c and d groups represent CR^1 or CR^2 ;

R^1 is selected from H or halo;

R^2 is selected from NO_2 , Br, Cl or I;

R^3 is Cl;

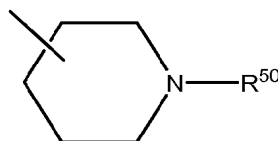
R^4 is H or halo;

R^5 , R^6 , R^7 and R^8 are H;

the dotted line between carbon atoms 5 and 6 represents an optional double bond, such that when a double bond is present, A and B independently represent H, and when no double bond is present between carbon atoms 5 and 6, A and B each independently represent H_2 ;

R^{20} and R^{21} are independently selected from H or alkyl;

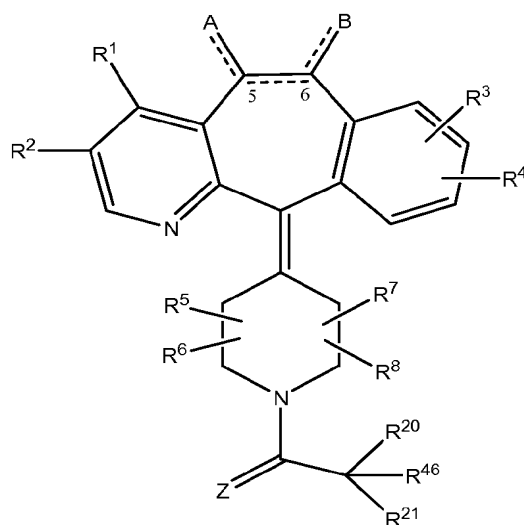
R^{46} is selected from: pyridyl, pyridyl N-oxide or piperidine Ring V:



wherein R^{50} represents alkyl, alkylcarbonyl, alkyloxycarbonyl, haloalkyl, or --
C(O)NH(R^{10}) wherein R^{10} is H or alkyl; and

Z represents O.

[00181] In one embodiment, R^1 is H. In one embodiment, R^2 is selected from Br, Cl or I. In one embodiment, R^2 is Br at the C-3 position. In one embodiment, R^2 is Br at the C-3 position and R^3 is at the C-8 position. In one embodiment, both R^{20} and R^{21} are hydrogen, or both R^{20} and R^{21} are alkyl. In one embodiment, both R^{20} and R^{21} are hydrogen. In one embodiment, R^{46} is 3-pyridyl, 4-pyridyl, 3-pyridyl N-oxide, 4-pyridyl N-oxide, 4-N-methyl piperidinyl, 3-N-methylpiperidinyl, 4-N-acetylpiperidinyl or 3-N-acetylpiperidinyl. In one embodiment, R^{46} is 3-pyridyl, 4-pyridyl, 3-pyridyl N-oxide, or 4-pyridyl N-oxide. In one embodiment, R^{46} is 4-pyridyl or 4-pyridyl N-oxide. In one embodiment, the compound may be any of the compounds shown in Figure 10. In another embodiment, the compound may be any of the compounds shown in Figure 11. In one embodiment, the compound is of the formula:



wherein:

R^1 is selected from H or halo;

R² is selected from --CH₃, Br, or I;

 R^3 is Cl;

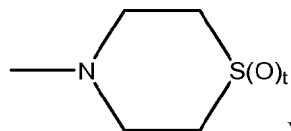
R⁴ is H or halo;

R^5, R^6, R^7 and R^8 are H;

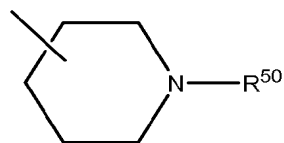
the dotted line between carbon atoms 5 and 6 represents an optional double bond, such that when a double bond is present, A and B independently represent H, and when no double bond is present between carbon atoms 5 and 6, A and B each independently represent H₂;

R^{20} and R^{21} are H:

R⁴⁶ is selected from: pyridyl, pyridyl N-oxide, triazolyl, 1-N-methylpiperazinyl,



wherein t is 0, 1 or 2, or piperidine Ring V:



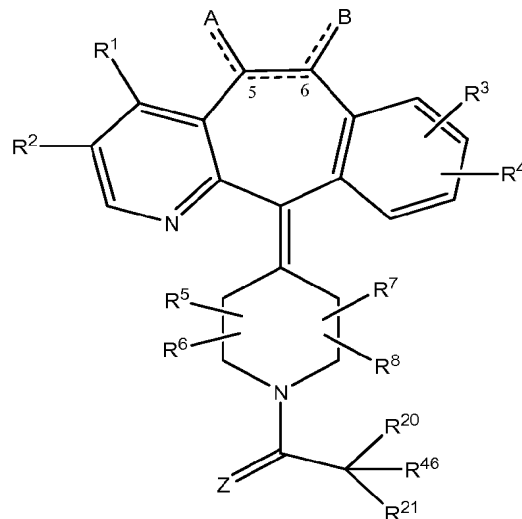
wherein R⁵⁰ represents alkyl, alkylcarbonyl, alkoxy carbonyl, H(R¹⁰) wherein R¹⁰ is H or alkyl; and

Z represents O.

[00182] In one embodiment, R¹ is H. In one embodiment, R² is selected from Br. In one embodiment, R² is Br and R³ is at the C-8 position. In one embodiment, R⁴⁶ is selected from

3-pyridyl, 4-pyridyl, 3-pyridyl N-oxide, 4-pyridyl N-oxide, 4-N-methyl piperidiny, 3-N-methylpiperidiny, 4-N-acetylpiperidiny or 3-N-acetylpiperidiny. In one embodiment, R^{46} is selected from: 3-pyridyl, 4-pyridyl, 3-pyridyl N-oxide, or 4-pyridyl N-oxide. In one embodiment, R^{46} is selected from 4-pyridyl or 4-pyridyl N-oxide. In one embodiment, the compound may be any of the compounds shown in Figure 12, Figure 13, or Figure 14.

[00183] In one aspect, the compound may have the formula:



wherein:

R^1 is selected from H or halo;

R^2 is Cl;

R^3 is Cl;

R^4 is H or halo;

R^5 , R^6 , R^7 and R^8 are H;

the dotted line between carbon atoms 5 and 6 represents an optional double bond, such that when a double bond is present, A and B independently represent H, and when no double bond is present between carbon atoms 5 and 6, A and B each independently represent H_2 ;

R^{20} and R^{21} are H;

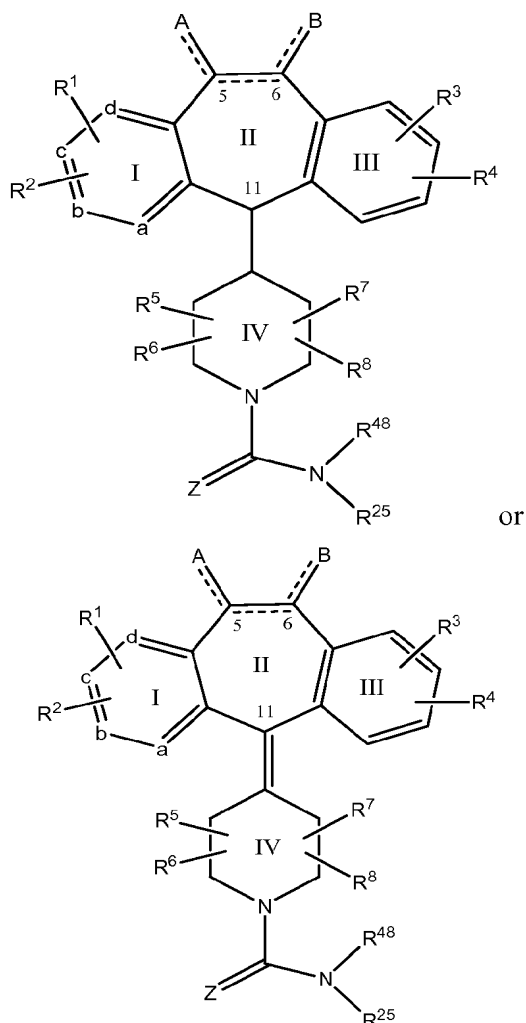
R^{46} is selected from: 4-pyridyl N-oxide, 4-pyridyl or piperidine Ring V:

wherein R^{50} represents alkyl, alkylcarbonyl, alkyloxycarbonyl, haloalkyl, or $--C(O)NH(R^{10})$ wherein R^{10} is H or alkyl; and

Z represents O.

[00184] In one embodiment, R^1 is H. In one embodiment, R^3 is at the C-8 position. In one embodiment, R^{46} is 4-pyridyl N-oxide, 4-N-methyl piperidiny, or 3-N-methylpiperidiny

[00185] In one aspect, the compound may be of the formula:



wherein: a represents N and the remaining b, c and d groups represent CR¹ or CR²;

R¹ and R² are independently selected from H, halo, --CF₃, lower alkyl or benzotriazol-1-yloxy;

R³ and R⁴ are independently selected from H or halo;

R⁵, R⁶, R⁷ and R⁸ are H;

the dotted line between carbon atoms 5 and 6 represents an optional double bond, such that when a double bond is present, A and B independently represent H, and when no double bond is present between carbon atoms 5 and 6, A and B each independently represent H₂;

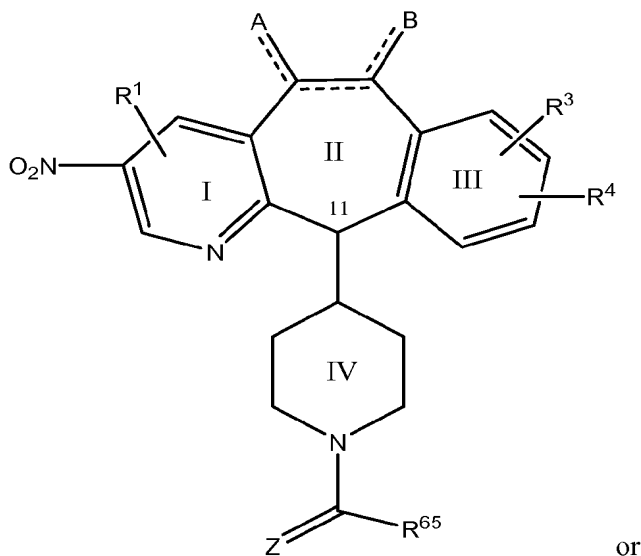
R²⁵ represents pyridyl, pyridyl N-oxide, N-methyl-piperidiny1 or phenyl;

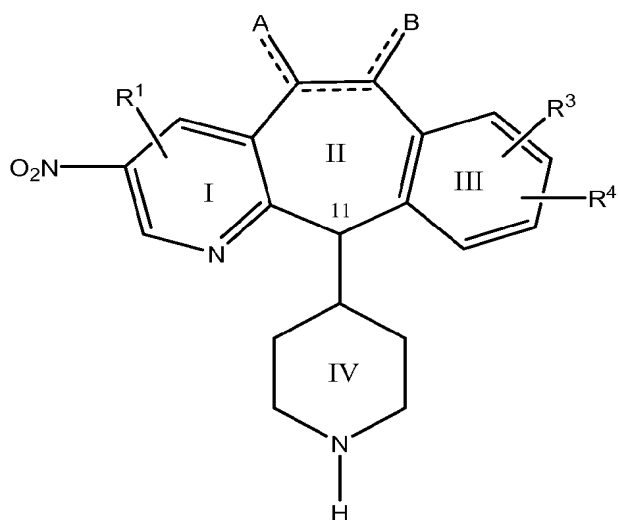
R⁴⁸ represents H or alkyl; and

Z represents O.

[00186] In one embodiment, R^1 is Cl or H; and R^2 is H, Cl or Br. In one embodiment, R^3 is Cl. In one embodiment, R^{25} represents phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyridyl N-oxide, 3-pyridyl N-oxide, or 4-pyridyl N-oxide. In one embodiment, R^{48} represents H or methyl. In one embodiment, R^{25} represents phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyridyl N-oxide, 3-pyridyl N-oxide, or 4-pyridyl N-oxide; and R^{48} represents H or methyl. In one embodiment, R^1 is Cl or H; R^2 is Br, Cl, or I; R^3 and R^4 independently represent H or halo; R^{25} represents phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyridyl N-oxide, 3-pyridyl N-oxide, or 4-pyridyl N-oxide; and R^{48} represents H or methyl. In one embodiment, R^3 is Cl at the C-8 position and R^4 is H. In one embodiment, the compound may have any structure shown in Figure 16, Figure 17, or Figure 18.

[00187] In one aspect, the compound may be of the formula:





wherein:

R^1 is selected from H or halo;

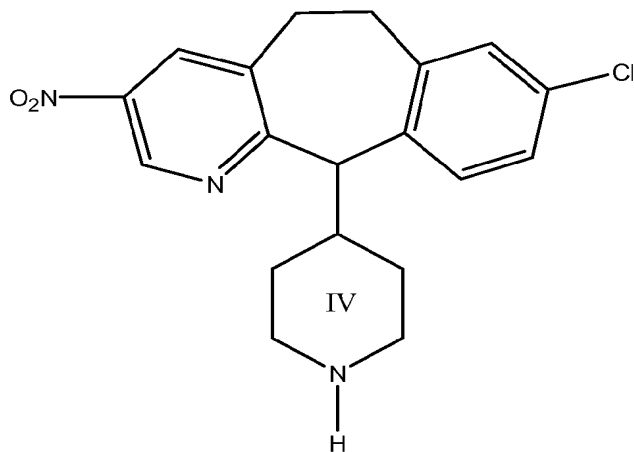
R^3 is Cl;

R^4 is H or halo;

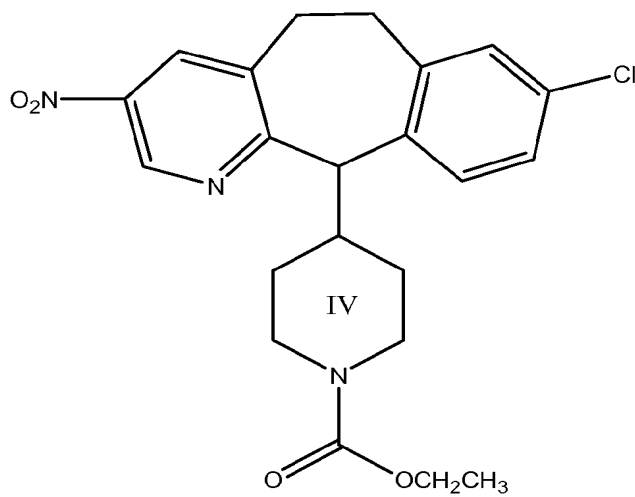
the dotted line between carbon atoms 5 and 6 represents an optional double bond, such that when a double bond is present, A and B independently represent H, and when no double bond is present between carbon atoms 5 and 6, A and B each independently represent H_2 ; and

R^{65} represents H or $--OR^{66}$ wherein R^{66} represents alkyl.

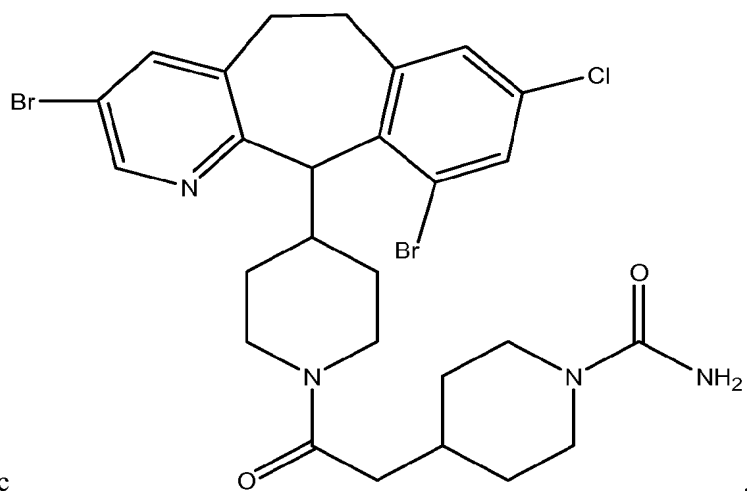
[00188] In one embodiment, the compound is:



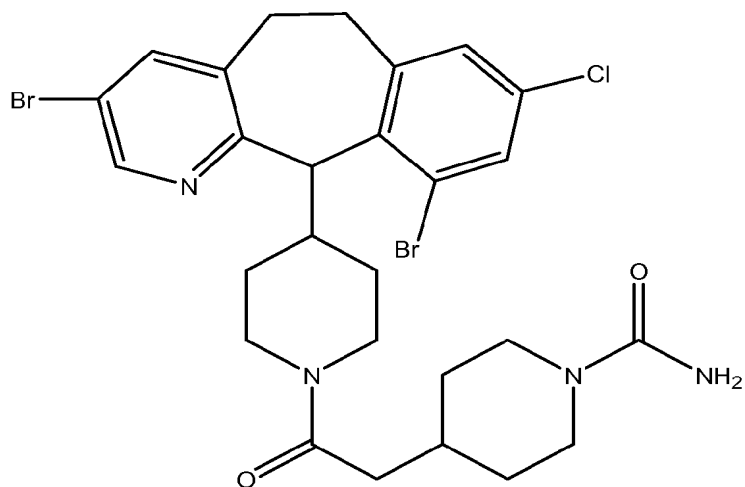
or

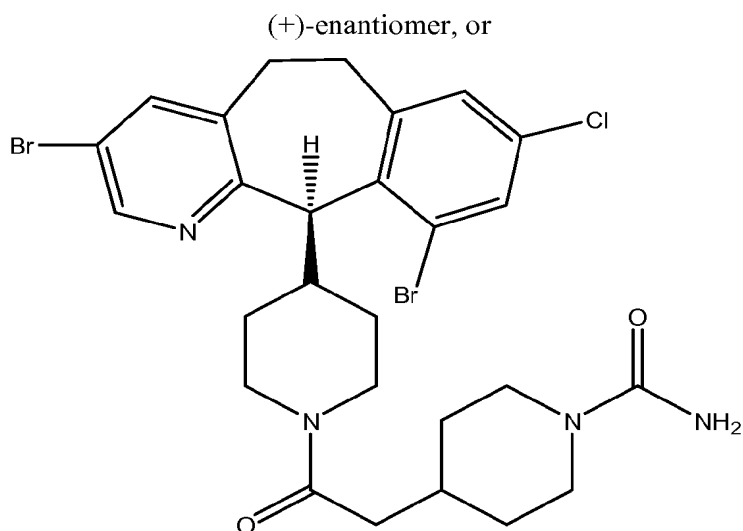


[00189] In certain embodiments, the compound is:

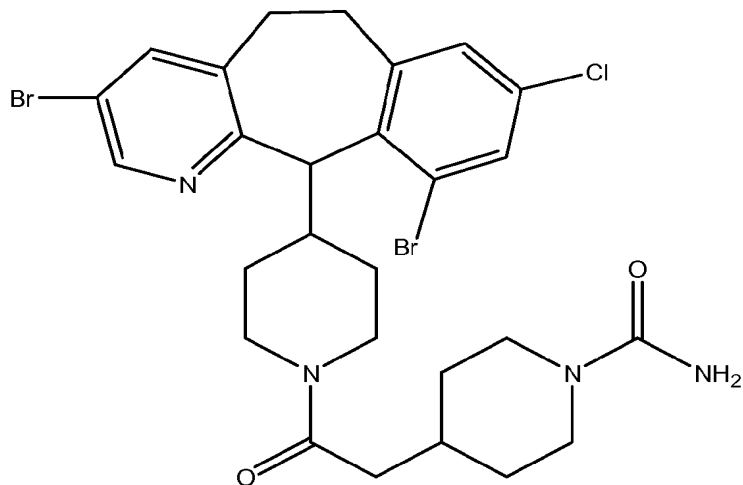


racemic

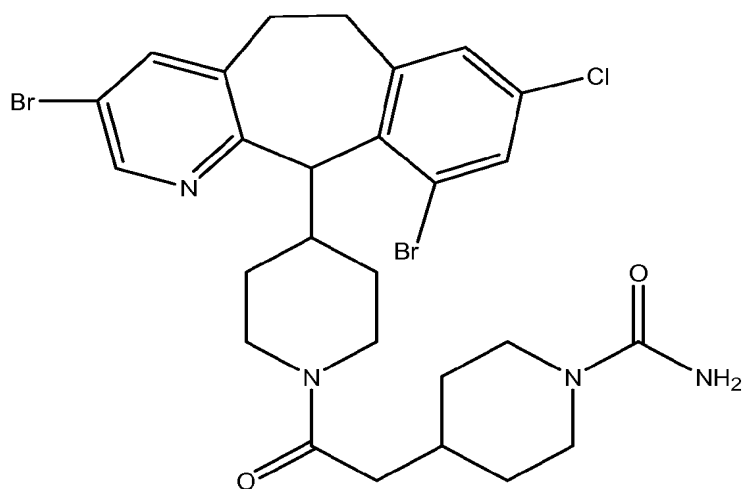




[00190] In another aspect, the invention provides a method of treating a subject with a lysosomal storage disease by administering a therapeutically effective amount of a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form of a farnesyl transferase inhibitor compound of the formula:

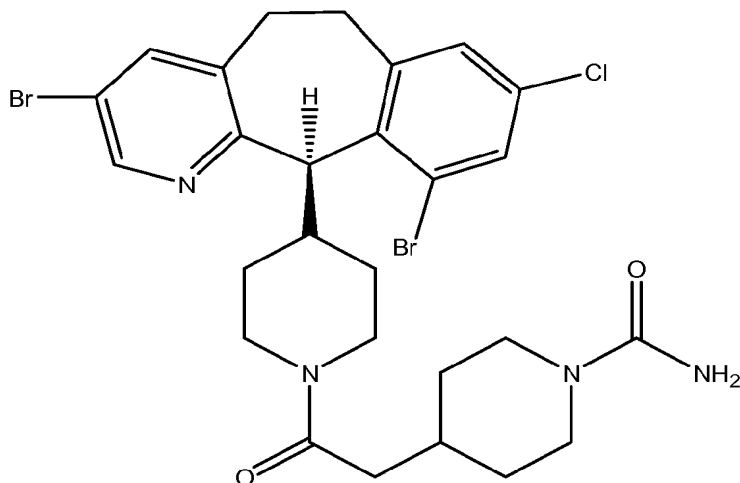


[00191] In another aspect, the invention provides a method of treating a subject with a lysosomal storage disease, by administering a therapeutically effective amount of a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form of a farnesyl transferase inhibitor compound of the formula:

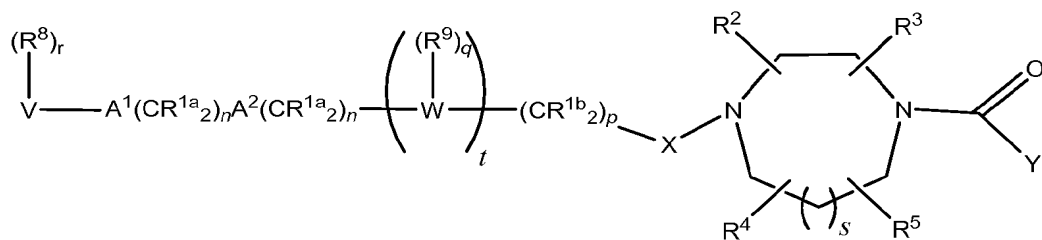


(+)-enantiomer.

[00192] In another aspect, the invention provides a method of treating a subject with a lysosomal storage disease by administering a therapeutically effective amount of a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form of a farnesyl transferase inhibitor compound of the formula:



[00193] In certain embodiments, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

wherein:

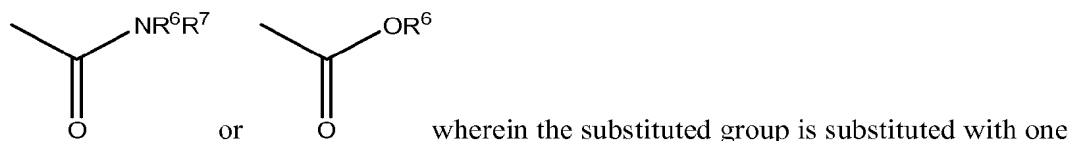
R^{1a} and R^{1b} are independently selected from:

a) hydrogen,

b) aryl, heterocycle, C_3 - C_{10} cycloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, R^{10} O-, R^{11} S(O)_m -, R^{10} C(O)NR¹⁰ -, $(R^{10})_2$ N-C(O)-, CN, NO₂, $(R^{10})_2$ N-C(NR¹⁰)-, R^{10} C(O)-, R^{10} OC(O)-, N₃, -N(R¹⁰)₂, or R^{11} OC(O)NR¹⁰ -,

c) unsubstituted or substituted C_1 - C_6 alkyl wherein the substituent on the substituted C_1 - C_6 alkyl is selected from unsubstituted or substituted aryl, heterocyclic, C_3 - C_{10} cycloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, R^{10} O-, R^{11} S(O)_m -, R^{10} C(O)NR¹⁰ -, $(R^{10})_2$ N-C(O) -, CN, $(R^{10})_2$ N-C(NR¹⁰)-, R^{10} C(O)-, R^{10} OC(O)-, N₃, -N(R¹⁰)₂, and R^{11} OC(O)-NR¹⁰ -;

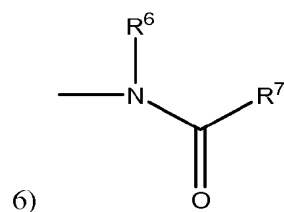
R^2 and R^3 are independently selected from: H; unsubstituted or substituted C_{1-8} alkyl, unsubstituted or substituted C_{2-8} alkenyl, unsubstituted or substituted C_{2-8} alkynyl, unsubstituted or substituted aryl, unsubstituted or substituted heterocycle,

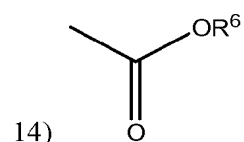
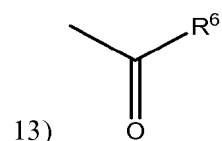
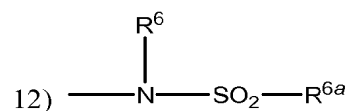
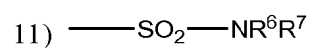
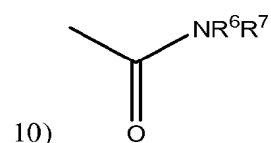
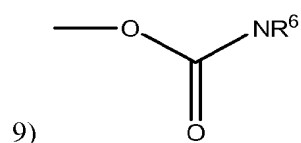
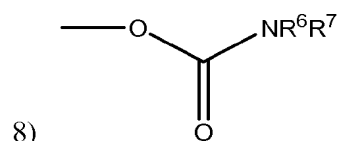
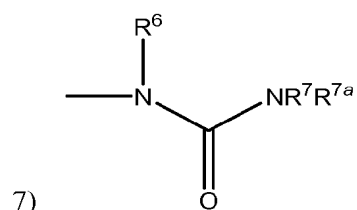


or more of: 1) aryl or heterocycle, unsubstituted or substituted with:

- a) C_{1-4} alkyl,
- b) $(CH_2)_p$ OR⁶,
- c) $(CH_2)_p$ NR⁶ R⁷,
- d) halogen,
- e) CN,

- 2) C_{3-6} cycloalkyl,
- 3) OR⁶,
- 4) SR^{6a}, S(O)R^{6a}, SO₂ R^{6a},
- 5) -NR⁶R⁷,





15) N₃ or

16) F; or

R² and R³ are attached to the same C atom and are combined to form -(CH₂)_n -

wherein one of the carbon atoms is optionally replaced by a moiety selected from:

O, S(O)_m, --NC(O)--, and --N(COR¹⁰)--;

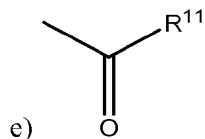
R⁴ and R⁵ are independently selected from H and CH₃ ;


and any two of R², R³, R⁴ and R⁵ are optionally attached to the same carbon atom;

R⁶, R⁷ and R^{7a} are independently selected from: H; C₁₋₄ alkyl, C₃₋₆ cycloalkyl,

heterocycle, aryl, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with:

a) C₁₋₄ alkoxy, b) aryl or heterocycle, c) halogen, d) HO,

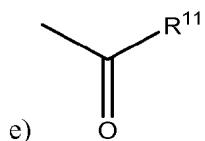



e) , f) --SO₂ R¹¹, or g) N(R¹⁰)₂; or

R⁶ and R⁷ may be joined in a ring;

R⁷ and R^{7a} may be joined in a ring;

R^{6a} is selected from: C₁₋₄ alkyl, C₃₋₆ cycloalkyl, heterocycle, aryl, unsubstituted or substituted with: a) C₁₋₄ alkoxy, b) aryl or heterocycle, c) halogen, d) HO,



e) , f) --SO₂ R¹¹, or g) N(R¹⁰)₂;

R⁸ is independently selected from:

a) hydrogen,

b) aryl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰ O--, R¹¹ S(O)_m-, R¹⁰ C(O)NR¹⁰-, (R¹⁰)₂ NC(O)--, R¹⁰₂ N-C(NR¹⁰)--, CN, NO₂, R¹⁰ C(O)--, R¹⁰ OC(O)--, N₃, --N(R¹⁰)₂, or R¹¹ OC(O)NR¹⁰-, and

c) C₁-C₆ alkyl unsubstituted or substituted by aryl, cyanophenyl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰ O--, R¹¹ S(O)_m-, R¹⁰ C(O)NH--, (R¹⁰)₂ NC(O)--, R¹⁰₂ N-C(NR¹⁰)--, CN, R¹⁰ C(O)--, R¹⁰ OC(O)--, N₃, --N(R¹⁰)₂, or R¹⁰ C(O)NH--;

R⁹ is selected from:

a) hydrogen,

b) C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰ O--, R¹¹ S(O)_m-, R¹⁰ C(O)NR¹⁰-, (R¹⁰)₂ NC(O)--, R¹⁰₂ N-C(NR¹⁰)--, CN, NO₂, R¹⁰ C(O)--, R¹⁰ OC(O)--, N₃, --N(R¹⁰)₂, or R¹¹ OC(O)NR¹⁰-, and

c) C₁-C₆ alkyl unsubstituted or substituted by perfluoroalkyl, F, Cl, Br, R¹⁰ O--, R¹¹ S(O)_m-, R¹⁰ C(O)NR¹⁰-, (R¹⁰)₂ NC(O)--, R¹⁰₂ N-C(NR¹⁰)--, CN, R¹⁰ C(O)--, R¹⁰ OC(O)--, N₃, --N(R¹⁰)₂, or R¹¹ OC(O)NR¹⁰-;

R¹⁰ is independently selected from hydrogen, C₁-C₆ alkyl, benzyl and aryl;

R¹¹ is independently selected from C₁-C₆ alkyl and aryl;

A¹ and A² are independently selected from: a bond, --CH=CH--, --C.tbd.C--, -C(O)--, --C(O)NR¹⁰-, --NR¹⁰ C(O)--, O, --N(R¹⁰)--,

$-\text{S}(\text{O})_2 \text{N}(\text{R}^{10})--$, $--\text{N}(\text{R}^{10})\text{S}(\text{O})_2-$, or $\text{S}(\text{O})_m$;

V is selected from: a) hydrogen, b) heterocycle, c) aryl, d) C_1 - C_{20} alkyl wherein from 0 to 4 carbon atoms are replaced with a heteroatom selected from O, S, and N, and e) C_2 - C_{20} alkenyl,

provided that V is not hydrogen if A^1 is $\text{S}(\text{O})_m$ and V is not hydrogen if A^1 is a bond, n is 0 and A^2 is $\text{S}(\text{O})_m$;

W is a heterocycle;

X is $--\text{CH}_2-$, $--\text{C}(=\text{O})--$, or $--\text{S}(=\text{O})_m-$;

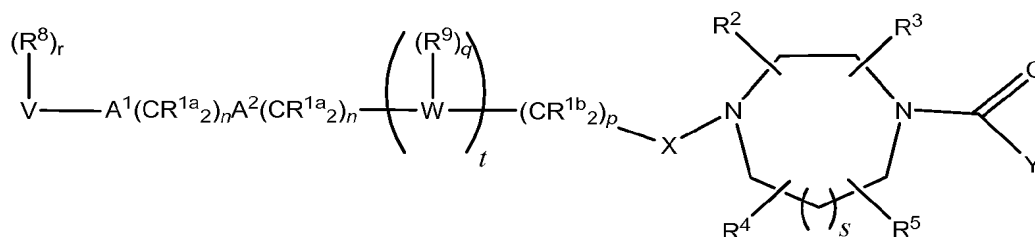
Y is unsubstituted or substituted aryl or unsubstituted or substituted heterocycle,

wherein the substituted aryl or substituted heterocycle is substituted with one or more of:

1) C_{1-4} alkyl, unsubstituted or substituted with: a) C_{1-4} alkoxy, b) $\text{NR}^6 \text{R}^7$, c) C_{3-6} cycloalkyl, d) aryl or heterocycle, e) HO, f) $--\text{S}(\text{O})_m \text{R}^{6a}$, or g) $--\text{C}(\text{O})\text{NR}^6 \text{R}^7$, 2) aryl or heterocycle, 3) halogen, 4) OR^6 , 5) $\text{NR}^6 \text{R}^7$, 6) CN, 7) NO_2 , 8) CF_3 , 9) $--\text{S}(\text{O})_m \text{R}^{6a}$, 10) $--\text{C}(\text{O})\text{NR}^6 \text{R}^7$, or 11) C_3 - C_6 cycloalkyl

m is 0, 1 or 2; n is 0, 1, 2, 3 or 4; p is 0, 1, 2, 3 or 4; q is 1 or 2; r is 0 to 5, provided that r is 0 when V is hydrogen; s is 0 or 1; t is 0 or 1; and u is 4 or 5.

[00194] In one embodiment, the compound may be of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

wherein:

R^{1a} is independently selected from: hydrogen or C_1 - C_6 alkyl;

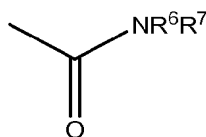
R^{1b} is independently selected from:

a) hydrogen,

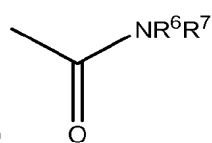
b) aryl, heterocycle, cycloalkyl, $\text{R}^{10} \text{O}-$, $-\text{N}(\text{R}^{10})_2$ or C_2 - C_6 alkenyl,

c) unsubstituted or substituted C_1 - C_6 alkyl wherein the substituent on the substituted C_1 - C_6 alkyl is selected from unsubstituted or substituted aryl, heterocycle, cycloalkyl, alkenyl, $\text{R}^{10} \text{O}-$ and $-\text{N}(\text{R}^{10})_2$;

R^3 , R^4 and R^5 are independently selected from H and CH_3 ;

R^2 is H;  or C_{1-5} alkyl, unbranched or branched, unsubstituted or substituted with one or more of:

- 1) aryl,
- 2) heterocycle,
- 3) OR^6 ,
- 4) SR^{6a} , $SO_2 R^{6a}$, or

5) 

and any two of R^2 , R^3 , R^4 , and R^5 are optionally attached to the same carbon atom;
 R^6 , R^7 and R^{7a} are independently selected from:

H; C_{1-4} alkyl, C_{3-6} cycloalkyl, aryl, heterocycle, unsubstituted or substituted with:

- a) C_{1-4} alkoxy,
- b) halogen, or
- c) aryl or heterocycle;

R^{6a} is selected from:

C_{1-4} alkyl or C_{3-6} cycloalkyl, unsubstituted or substituted with:

- a) C_{1-4} alkoxy,
- b) halogen, or
- c) aryl or heterocycle;

R^8 is independently selected from:

- a) hydrogen,
- b) C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 perfluoroalkyl, F, Cl, $R^{10}O-$, $R^{10}C(O)NR^{10}-$, CN, NO_2 , $(R^{10})_2N-C(NR^{10})-$, $R^{10}C(O)-$, $R^{10}OC(O)-$, $--N(R^{10})_2$, or $R^{11}OC(O)NR^{10}-$, and
- c) C_1 - C_6 alkyl substituted by C_1 - C_6 perfluoroalkyl, $R^{10}O-$, $R^{10}C(O)NR^{10}-$, $(R^{10})_2N-C(NR^{10})-$, $R^{10}C(O)-$, $R^{10}OC(O)-$, $--N(R^{10})_2$, or $R^{11}OC(O)NR^{10}-$;

R^9 is selected from:

- a) hydrogen,

b) C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 perfluoroalkyl, F, Cl, $R^{10}O-$, $R^{11}S(O)_m-$, $R^{10}C(O)NR^{10}-$, CN, NO_2 , $(R^{10})_2N-C(NR^{10})-$, $R^{10}C(O)-$, $R^{10}OC(O)-$, $--N(R^{10})_2$, or $R^{11}OC(O)NR^{10}-$, and

c) C_1-C_6 alkyl unsubstituted or substituted by C_1-C_6 perfluoroalkyl, F, Cl, $R^{10}O-$, $R^{11}S(O)_m-$, $R^{10}C(O)NR^{10}-$, CN, $(R^{10})_2N-C(NR^{10})-$, $R^{10}C(O)-$, $R^{10}OC(O)-$, $--N(R^{10})_2$, or $R^{11}OC(O)NR^{10}-$;

R^{10} is independently selected from hydrogen, C_1-C_6 alkyl, benzyl and aryl;

R^{11} is independently selected from C_1-C_6 alkyl and aryl;

A^1 and A^2 are independently selected from: a bond, $--CH=CH-$, $--C.tbd.C-$, $--C(O)-$, $--C(O)NR^{10}-$, O, $--N(R^{10})-$, or $S(O)_m$;

V is selected from:

a) hydrogen,

b) heterocycle selected from pyrrolidinyl, imidazolyl, pyridinyl, thiazolyl, pyridonyl, 2-oxopiperidinyl, indolyl, quinolinyl, isoquinolinyl, and thienyl,

c) aryl,

d) C_1-C_{20} alkyl wherein from 0 to 4 carbon atoms are replaced with a heteroatom selected from O, S, and N, and

e) C_2-C_{20} alkenyl, and

provided that V is not hydrogen if A^1 is $S(O)_m$ and V is not hydrogen if A^1 is a bond, n is 0 and A^2 is $S(O)_m$;

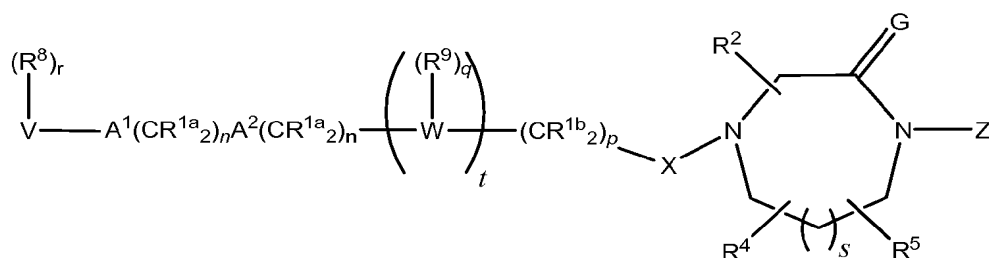
W is a heterocycle selected from pyrrolidinyl, imidazolyl, pyridinyl, thiazolyl, pyridonyl, 2-oxopiperidinyl, indolyl, quinolinyl, or isoquinolinyl;

X is $--CH_2-$ or $--C(=O)-$;

Y is mono- or bicyclic aryl, or mono- or bicyclic heterocycle, unsubstituted or substituted with one or more of: a) C_{1-4} alkyl, b) C_{1-4} alkoxy, c) halogen, or d) NR^6R^7 ;

m is 0, 1 or 2; n is 0, 1, 2, 3 or 4; p is 0, 1, 2, 3 or 4; r is 0 to 5, provided that r is 0 when V is hydrogen; s is 0 or 1; and t is 0 or 1.

[00195] In certain embodiments, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the formula:



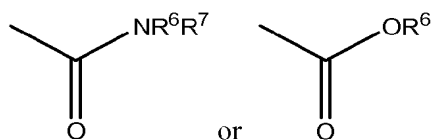
or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

wherein:

R^{1a} and R^{1b} are independently selected from:

- a) hydrogen,
- b) aryl, heterocycle, C_3 - C_{10} cycloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, R^{10} O--, R^{11} S(O)_m-, R^{10} C(O)NR¹⁰-, CN(R¹⁰)₂ NC(O)--, R^{10}_2 N-C(NR¹⁰)--, CN, NO₂, R^{10} C(O)--, R^{10} OC(O)--, N₃, --N(R¹⁰)₂, or R^{11} OC(O)NR¹⁰-,
- c) unsubstituted or substituted C_1 - C_6 alkyl wherein the substituent on the substituted C_1 - C_6 alkyl is selected from unsubstituted or substituted aryl, heterocyclic, C_3 - C_{10} cycloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, R^{10} O--, R^{11} S(O)_m-, R^{10} C(O)NR¹⁰-, (R¹⁰)₂ NC(O)--, R^{10}_2 N-C(NR¹⁰)--, CN, R^{10} C(O)--, R^{10} OC(O)--, N₃, --N(R¹⁰)₂, and R^{11} OC(O)-NR¹⁰-;

R^2 and R^3 are independently selected from: H; unsubstituted or substituted C_{1-8} alkyl, unsubstituted or substituted C_{2-8} alkenyl, unsubstituted or substituted C_{2-8} alkynyl, unsubstituted or substituted aryl, unsubstituted or substituted heterocycle,



wherein the substituted group is substituted with one

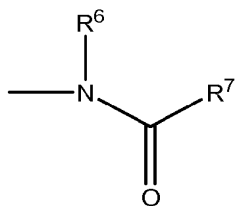
or more of: 1) aryl or heterocycle, unsubstituted or substituted with:

- a) C_{1-4} alkyl,
- b) $(CH_2)_p$ OR⁶,
- c) $(CH_2)_p$ NR⁶ R⁷,
- d) halogen,
- e) CN,

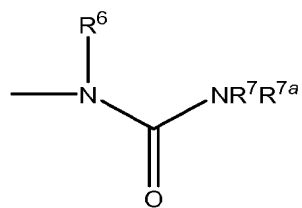
2) C_{3-6} cycloalkyl,

3) OR⁶,

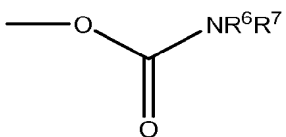
4) SR^{6a}, S(O)R^{6a}, SO₂ R^{6a},

5) $-\text{NR}^6\text{R}^7$,

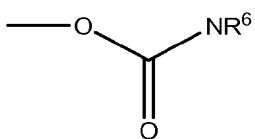
6)



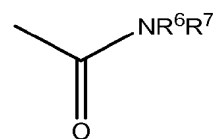
7)



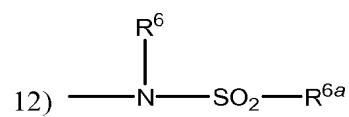
8)



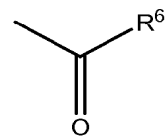
9)



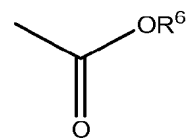
10)

11) $\text{---SO}_2\text{---NR}^6\text{R}^7$ 

12)



13)



14)

15) N_3 or16) F ; or

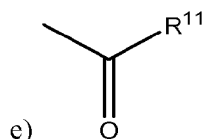
R^2 and R^3 are attached to the same C atom and are combined to form $-(CH_2)_u$ - wherein one of the carbon atoms is optionally replaced by a moiety selected from: O, $S(O)_m$, $-NC(O)-$, and $-N(COR^{10})-$;

R^4 is selected from H and CH_3 ;

and any two of R^2 , R^3 and R^4 are optionally attached to the same carbon atom;

R^6 , R^7 and R^{7a} are independently selected from: H; C_{1-4} alkyl, C_{3-6} cycloalkyl, heterocycle, aryl, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with:

- a) C_{1-4} alkoxy,
- b) aryl or heterocycle,
- c) halogen,
- d) HO,



f) $-SO_2 R^{11}$, or

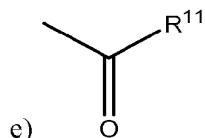
g) $N(R^{10})_2$; or

R^6 and R^7 may be joined in a ring;

R^7 and R^{7a} may be joined in a ring;

R^{6a} is selected from: C_{1-4} alkyl, C_{3-6} cycloalkyl, heterocycle, aryl, unsubstituted or substituted with:

- a) C_{1-4} alkoxy,
- b) aryl or heterocycle,
- c) halogen,
- d) HO,



f) $-SO_2 R^{11}$, or

g) $N(R^{10})_2$;

R^8 is independently selected from:

- a) hydrogen,

b) aryl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰ O--, R¹¹ S(O)_m-, R¹⁰ C(O)NR¹⁰-, (R¹⁰)₂ NC(O)--, R¹⁰₂ N-C(NR¹⁰)--, CN, NO₂, R¹⁰ C(O)-, R¹⁰ OC(O)-, N₃, --N(R¹⁰)₂, or R¹¹ OC(O)NR¹⁰-, and

c) C₁-C₆ alkyl unsubstituted or substituted by aryl, cyanophenyl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰ O-, R¹¹ S(O)_m-, R¹⁰ C(O)NH-, (R¹⁰)₂ NC(O)-, R¹⁰₂ N-C(NR¹⁰)-, CN, R¹⁰ C(O)-, R¹⁰ OC(O)-, N₃, -N(R¹⁰)₂, or R¹⁰ C(O)NH-;

R⁹ is selected from:

a) hydrogen,

b) alkenyl, alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰ O--, R¹¹ S(O)_m-, R¹⁰ C(O)NR¹⁰-, (R¹⁰)₂ NC(O)--, R¹⁰₂ N-C(NR¹⁰)--, CN, NO₂, R¹⁰ C(O)--, R¹⁰ OC(O)--, N₃, --N(R¹⁰)₂, or R¹¹ OC(O)NR¹⁰-, and

c) C₁-C₆ alkyl unsubstituted or substituted by perfluoroalkyl, F, Cl, Br, R¹⁰ O--, R¹¹ S(O)_m-, R¹⁰ C(O)NR¹⁰-, (R¹⁰)₂ NC(O)--, R¹⁰₂ N-C(NR¹⁰)--, CN, R¹⁰ C(O)--, R¹⁰ OC(O)--, N₃, --N(R¹⁰)₂, or R¹¹ OC(O)NR¹⁰-;

R¹⁰ is independently selected from hydrogen, C₁-C₆ alkyl, benzyl and aryl;

R¹¹ is independently selected from C₁-C₆ alkyl and aryl;

A¹ and A² are independently selected from: a bond, --CH=CH--, --C.tbd.C--, --C(O)-, -C(O)NR¹⁰-, --NR¹⁰ C(O)--, O, --N(R¹⁰)--, --S(O)₂ N(R¹⁰)--, --N(R¹⁰)S(O)₂-, or S(O)_m;

G is H₂ or O;

V is selected from:

a) hydrogen,

b) heterocycle,

c) aryl,

d) C₁-C₂₀ alkyl wherein from 0 to 4 carbon atoms are replaced with a heteroatom selected from O, S, and N, and

e) C₂-C₂₀ alkenyl,

provided that V is not hydrogen if A¹ is S(O)_m and V is not hydrogen if A¹ is a bond, n is 0 and A² is S(O)_m;

W is a heterocycle;

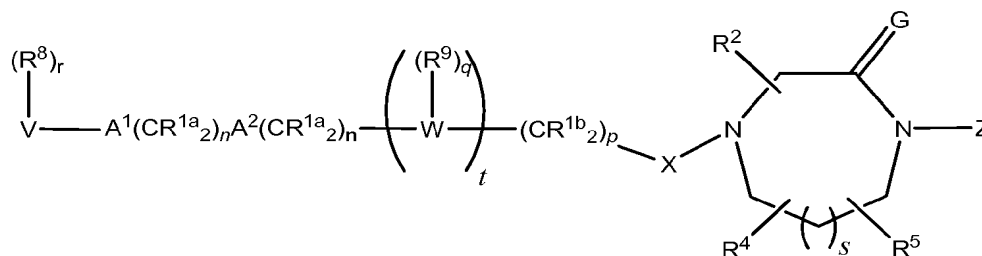
X is --CH₂-, --C(=O)--, or --S(=O)_m-;

Z is a unsubstituted or substituted group selected from aryl, heteroaryl, arylmethyl, heteroarylmethyl, arylsulfonyl, heteroarylsulfonyl, wherein the substituted group is substituted with one or more of the following:

1) C₁₋₄ alkyl, unsubstituted or substituted with: a) C₁₋₄ alkoxy, b) NR⁶R⁷, c) C₃₋₆ cycloalkyl, d) aryl or heterocycle, e) HO, f) --S(O)_mR^{6a}, or g) --C(O)NR⁶R⁷, 2) aryl or heterocycle, 3) halogen, 4) OR⁶, 5) NR⁶R⁷, 6) CN, 7) NO₂, 8) CF₃, 9) --S(O)_mR^{6a}, 10) --C(O)NR⁶R⁷, or 11) C₃-C₆ cycloalkyl;

m is 0, 1 or 2; n is 0, 1, 2, 3 or 4; p is 0, 1, 2, 3 or 4; q is 1 or 2; r is 0 to 5, provided that r is 0 when V is hydrogen; s is 0 or 1; t is 0 or 1; and u is 4 or 5.

[00196] In one embodiment, the compound may be of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

wherein:

R^{1a} is independently selected from: hydrogen or C₁-C₆ alkyl;

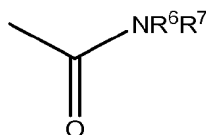
R^{1b} is independently selected from:

a) hydrogen,

b) aryl, heterocycle, cycloalkyl, R¹⁰ O--, --N(R¹⁰)₂ or C₂-C₆ alkenyl,

c) unsubstituted or substituted C₁-C₆ alkyl wherein the substituent on the substituted C₁-C₆ alkyl is selected from unsubstituted or substituted aryl, heterocycle, cycloalkyl, alkenyl, R¹⁰ O-- and --N(R¹⁰)₂;

R³ and R⁴ are independently selected from H and CH₃;

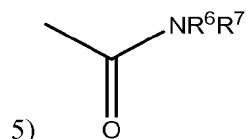
R² is H;  or C₁₋₅ alkyl, unbranched or branched, unsubstituted or substituted with one or more of:

1) aryl,

2) heterocycle,

3) OR⁶,

4) SR^{6a} , $\text{SO}_2 \text{R}^{6a}$, or



and any two of R^2 , R^3 , R^4 , and R^5 are optionally attached to the same carbon atom;

R^6 , R^7 and R^{7a} are independently selected from:

H; C_{1-4} alkyl, C_{3-6} cycloalkyl, aryl, heterocycle, unsubstituted or substituted with:

- a) C_{1-4} alkoxy,
- b) halogen, or
- c) aryl or heterocycle;

R^{6a} is selected from:

C_{1-4} alkyl or C_{3-6} cycloalkyl, unsubstituted or substituted with:

- a) C_{1-4} alkoxy,
- b) halogen, or
- c) aryl or heterocycle;

R^8 is independently selected from:

- a) hydrogen,
- b) C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 perfluoroalkyl, F, Cl, $\text{R}^{10} \text{O}-$, $\text{R}^{10} \text{C}(\text{O})\text{NR}^{10}-$, CN, NO_2 , $(\text{R}^{10})_2 \text{N}-\text{C}(\text{NR}^{10})-$, $\text{R}^{10} \text{C}(\text{O})-$, $\text{R}^{10} \text{OC}(\text{O})-$, $-\text{N}(\text{R}^{10})_2$, or $\text{R}^{11} \text{OC}(\text{O})\text{NR}^{10}-$, and
- c) C_1 - C_6 alkyl substituted by C_1 - C_6 perfluoroalkyl, $\text{R}^{10} \text{O}-$, $\text{R}^{10} \text{C}(\text{O})\text{NR}^{10}-$, $(\text{R}^{10})_2 \text{N}-\text{C}(\text{NR}^{10})-$, $\text{R}^{10} \text{C}(\text{O})-$, $\text{R}^{10} \text{OC}(\text{O})-$, $-\text{N}(\text{R}^{10})_2$, or $\text{R}^{11} \text{OC}(\text{O})\text{NR}^{10}-$;

R^9 is selected from:

- a) hydrogen,
- b) C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 perfluoroalkyl, F, Cl, $\text{R}^{10} \text{O}-$, $\text{R}^{11} \text{S}(\text{O})_m-$, $\text{R}^{10} \text{C}(\text{O})\text{NR}^{10}-$, CN, NO_2 , $(\text{R}^{10})_2 \text{N}-\text{C}(\text{NR}^{10})-$, $\text{R}^{10} \text{C}(\text{O})-$, $\text{R}^{10} \text{OC}(\text{O})-$, $-\text{N}(\text{R}^{10})_2$, or $\text{R}^{11} \text{OC}(\text{O})\text{NR}^{10}-$, and
- c) C_1 - C_6 alkyl unsubstituted or substituted by C_1 - C_6 perfluoroalkyl, F, Cl, $\text{R}^{10} \text{O}-$, $\text{R}^{11} \text{S}(\text{O})_m-$, $\text{R}^{10} \text{C}(\text{O})\text{NR}^{10}-$, CN, $(\text{R}^{10})_2 \text{N}-\text{C}(\text{NR}^{10})-$, $\text{R}^{10} \text{C}(\text{O})-$, $\text{R}^{10} \text{OC}(\text{O})-$, $-\text{N}(\text{R}^{10})_2$, or $\text{R}^{11} \text{OC}(\text{O})\text{NR}^{10}-$;

R^{10} is independently selected from hydrogen, C_1 - C_6 alkyl, benzyl and aryl;

R^{11} is independently selected from C_1 - C_6 alkyl and aryl;

A^1 and A^2 are independently selected from: a bond, $--CH=CH--$, $--C.tbd.C--$, $--C(O)--$, $--C(O)NR^{10}-$, O, $--N(R^{10})--$, or $S(O)_m$;

V is selected from:

- a) hydrogen,
- b) heterocycle selected from pyrrolidinyl, imidazolyl, pyridinyl, thiazolyl, pyridonyl, 2-oxopiperidinyl, indolyl, quinolinyl, isoquinolinyl, and thienyl,
- c) aryl,
- d) C_1-C_{20} alkyl wherein from 0 to 4 carbon atoms are replaced with a heteroatom selected from O, S, and N, and
- e) C_2-C_{20} alkenyl, and provided that V is not hydrogen if A^1 is $S(O)_m$ and V is not hydrogen if A^1 is a bond, n is 0 and A^2 is $S(O)_m$;

G is H_2 or O;

W is a heterocycle selected from pyrrolidinyl, imidazolyl, pyridinyl, thiazolyl, pyridonyl, 2-oxopiperidinyl, indolyl, quinolinyl, or isoquinolinyl;

X is $--CH_2-$ or $--C(=O)--$;

Z is mono- or bicyclic aryl, mono- or bicyclic heteroaryl, mono- or bicyclic arylmethyl, mono- or bicyclic heteroarylmethyl, mono- or bicyclic arylsulfonyl, mono- or bicyclic heteroarylsulfonyl, unsubstituted or substituted with one or two of the following:

- 1) C_{1-4} alkyl, unsubstituted or substituted with: a) C_{1-4} alkoxy, b) $NR^6 R^7$, c) C_{3-6} cycloalkyl, d) aryl or heterocycle, e) HO, f) $--S(O)_m R^6$, or g) $--C(O)NR^6 R^7$; 2) aryl or heterocycle, 3) halogen, 4) OR^6 , 5) $NR^6 R^7$, 6) CN, 7) NO_2 , 8) CF_3 , 9) $--S(O)_m R^6$, 10) $--C(O)NR^6 R^7$, or 11) C_3-C_6 cycloalkyl;

m is 0, 1 or 2; n is 0, 1, 2, 3 or 4; p is 0, 1, 2, 3 or 4; r is 0 to 5, provided that r is 0 when V is hydrogen; s is 0 or 1; t is 0 or 1; and u is 4 or 5;

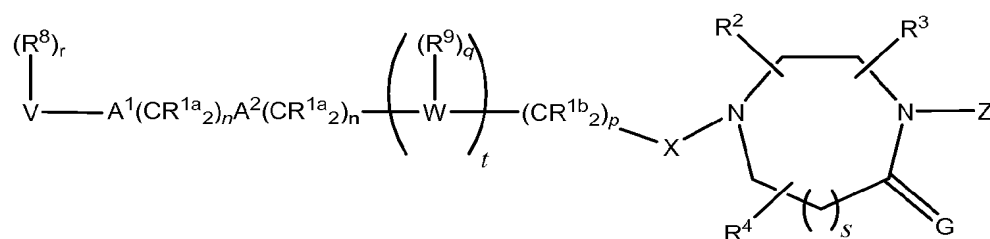
provided that when G is H_2 and W is imidazolyl, then the substituent $(R^8)_r - V--A^1$

$(CR^{1a_2})_n A^2 (CR^{1a_2})_n$ - is not H and

provided that when X is $--C(=O)--$, or $--S(=O)_m-$, then t is 1 and the substituent $(R^8)_r -$

$V--A^1 (CR^{1a_2})_n A^2 (CR^{1a_2})_n$ - is not H.

[00197] In certain embodiments, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

wherein:

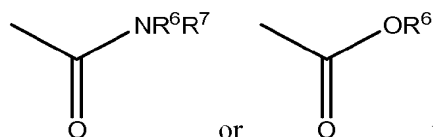
R^{1a} and R^{1b} are independently selected from:

a) hydrogen,

b) aryl, heterocycle, C_3 - C_{10} cycloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, R^{10} O--, R^{11} S(O)_m-, R^{10} C(O)NR¹⁰-, (R^{10})₂ NC(O)--, R^{10}_2 N-C(NR¹⁰)--, CN, NO₂, R^{10} C(O)--, R^{10} OC(O)--, N₃, --N(R^{10})₂ or R^{11} OC(O)NR¹⁰-,

c) unsubstituted or substituted C_1 - C_6 alkyl wherein the substituent on the substituted C_1 - C_6 alkyl is selected from unsubstituted or substituted aryl, heterocyclic, C_3 - C_{10} cycloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, R^{10} O--, R^{11} S(O)_m-, R^{10} C(O)NR¹⁰-, (R^{10})₂ NC(O)--, R^{10}_2 N-C(NR¹⁰)--, CN, R^{10} C(O)--, R^{10} OC(O)--, N₃, --N(R^{10})₂, and R^{11} OC(O)-NR¹⁰-;

R^2 and R^3 are independently selected from: H; unsubstituted or substituted C_{1-8} alkyl, unsubstituted or substituted C_{2-8} alkenyl, unsubstituted or substituted C_{2-8} alkynyl, unsubstituted or substituted aryl, unsubstituted or substituted heterocycle,



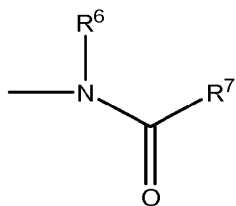
wherein the substituted group is substituted with one or more of: 1) aryl or heterocycle, unsubstituted or substituted with:

- a) C_{1-4} alkyl,
- b) $(CH_2)_p$ OR⁶,
- c) $(CH_2)_p$ NR⁶ R⁷,
- d) halogen,
- e) CN,

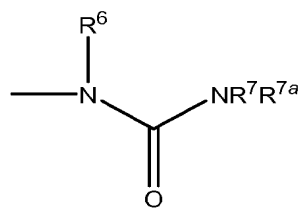
2) C_{3-6} cycloalkyl,

3) OR⁶,

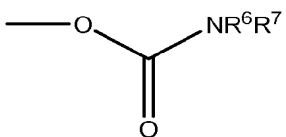
4) SR^{6a}, S(O)R^{6a}, SO₂ R^{6a},

5) $-\text{NR}^6\text{R}^7$,

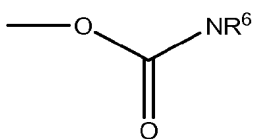
6)



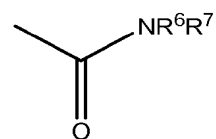
7)



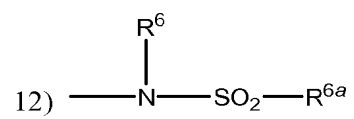
8)



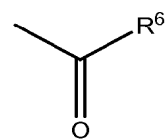
9)



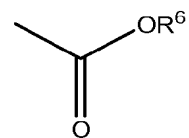
10)

11) $\text{---SO}_2\text{---NR}^6\text{R}^7$ 

12)



13)



14)

15) N_3 or16) F ; or

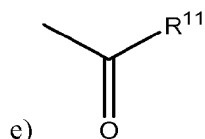
R^2 and R^3 are attached to the same C atom and are combined to form $-(CH_2)_u-$ wherein one of the carbon atoms is optionally replaced by a moiety selected from: O, $S(O)_m$, $NC(O)-$, and $-N(COR^{10})-$;

R^4 is selected from H and CH_3 ;

and any two of R^2 , R^3 and R^4 are optionally attached to the same carbon atom;

R^6 , R^7 and R^{7a} are independently selected from: H; C_{1-4} alkyl, C_{3-6} cycloalkyl, heterocycle, aryl, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with:

- a) C_{1-4} alkoxy,
- b) aryl or heterocycle,
- c) halogen,
- d) HO,



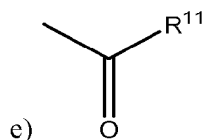
- f) $-SO_2 R^{11}$, or g) $N(R^{10})_2$; or

R^6 and R^7 may be joined in a ring;

R^7 and R^{7a} may be joined in a ring;

R^{6a} is selected from: C_{1-4} alkyl, C_{3-6} cycloalkyl, heterocycle, aryl, unsubstituted or substituted with:

- a) C_{1-4} alkoxy,
- b) aryl or heterocycle,
- c) halogen,
- d) HO,



- f) $-SO_2 R^{11}$, or
- g) $N(R^{10})_2$;

R^8 is independently selected from:

- a) hydrogen,

b) aryl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰ O--, R¹¹ S(O)_m -, R¹⁰ C(O)NR¹⁰ -, (R¹⁰)₂ NC(O)--, R¹⁰₂ N-C(NR¹⁰)--, CN, NO₂, R¹⁰ C(O)--, R¹⁰ OC(O)--, N₃, --N(R¹⁰)₂, or R¹¹ OC(O)NR¹⁰ -, and

c) C₁-C₆ alkyl unsubstituted or substituted by aryl, cyanophenyl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰ O--, R¹¹ S(O)_m -, R¹⁰ C(O)NH--, (R¹⁰)₂ NC(O)--, R¹⁰₂ N-C(NR¹⁰)--, CN, R¹⁰ C(O)--, R¹⁰ OC(O)--, N₃, --N(R¹⁰)₂, or R¹⁰ OC(O)NH--;

R⁹ is selected from:

a) hydrogen,

b) C₂-C₆ alkenyl, C₂-C₆ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰ O--, R¹¹ S(O)_m -, R¹⁰ C(O)NR¹⁰ -, (R¹⁰)₂ NC(O)--, R¹⁰₂ N-C(NR¹⁰)--, CN, NO₂, R¹⁰ C(O)--, R¹⁰ OC(O)--, N₃, --N(R¹⁰)₂, or R¹¹ OC(O)NR¹⁰ -, and

c) C₁-C₆ alkyl unsubstituted or substituted by perfluoroalkyl, F, Cl, Br, R¹⁰ O--, R¹¹ S(O)_m -, R¹⁰ C(O)NR¹⁰ -, (R¹⁰)₂ NC(O)--, R¹⁰₂ N-C(NR¹⁰)--, CN, R¹⁰ C(O)--, R¹⁰ OC(O)--, N₃, --N(R¹⁰)₂, or R¹¹ OC(O)NR¹⁰ -;

R¹⁰ is independently selected from hydrogen, C₁-C₆ alkyl, benzyl and aryl;

R¹¹ is independently selected from C₁-C₆ alkyl and aryl;

A¹ and A² are independently selected from: a bond, --CH=CH--, --C.tbd.C--, --C(O)--, --C(O)NR¹⁰ -, --NR¹⁰ C(O)--, O, --N(R¹⁰)--, --S(O)₂ N(R¹⁰)--, --N(R¹⁰)S(O)₂ -, or S(O)_m ;

G is O;

V is selected from:

a) hydrogen,

b) heterocycle,

c) aryl,

d) C₁-C₂₀ alkyl wherein from 0 to 4 carbon atoms are replaced with a heteroatom selected from O, S, and N, and

e) C₂-C₂₀ alkenyl,

provided that V is not hydrogen if A¹ is S(O)_m and V is not hydrogen if A¹ is a bond, n is 0 and A² is S(O)_m ;

W is a heterocycle;

X is --CH₂ -, --C(=O)--, or --S(=O)_m -;

Z is a unsubstituted or substituted group selected from aryl, heteroaryl, arylmethyl, heteroarylmethyl, arylsulfonyl, heteroarylsulfonyl, wherein the substituted group is substituted with one or more of the following:

1) C₁₋₄ alkyl, unsubstituted or substituted with: a) C₁₋₄ alkoxy, b) NR⁶ R⁷, c) C₃₋₆ cycloalkyl, d) aryl or heterocycle, e) HO, f) --S(O)_m R^{6a}, or g) --C(O)NR⁶ R⁷, 2) aryl or heterocycle, 3) halogen, 4) OR⁶, 5) NR⁶ R⁷, 6) CN, 7) NO₂, 8) CF₃, 9) --S(O)_m R^{6a}, 10) --C(O)NR⁶ R⁷, or 11) C₃-C₆ cycloalkyl;

m is 0, 1 or 2; n is 0, 1, 2, 3 or 4; p is 0, 1, 2, 3 or 4; q is 1 or 2; r is 0 to 5, provided that r is 0 when V is hydrogen; s is 1; t is 0 or 1; and u is 4 or 5.

[00198] In certain embodiments, the invention provides a method of treating a subject with a lysosomal storage disease by administering one or more of the following farnesyl transferase inhibitor compounds:

2(S)-Butyl-1-(2,3-diaminoprop-1-yl)-4-(1-naphthoyl)piperazine
 1-(3-Amino-2-(2-naphthylmethylamino)prop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine
 2(S)-Butyl-1-{5-[1-(2-naphthylmethyl)]-4,5-dihydroimidazol}methyl-4-(1-naphthoyl)piperazine
 1-[5-(1-Benzylimidazol)methyl]-2(S)-butyl-4-(1-naphthoyl)piperazine
 1-{5-[1-(4-Nitrobenzyl)imidazolyl]methyl}-2(S)-butyl-4-(1-naphthoyl)piperazine
 1-(3-Acetamidomethylthio-2(R)-aminoprop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine
 2(S)-Butyl-1-[2-(1-imidazolyl)ethyl]sulfonyl-4-(1-naphthoyl)piperazine
 2(R)-Butyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine
 2(S)-Butyl-4-(1-naphthoyl)-1-(3-pyridylmethyl)piperazine
 1-2(S)-butyl-(2(R)-(4-nitrobenzyl)amino-3-hydroxypropyl)-4-(1-naphthoyl)piperazine
 1-(2(R)-Amino-3-hydroxyheptadecyl)-2(S)-butyl-4-(1-naphthoyl)piperazine
 2(S)-Benzyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine
 1-(2(R)-Amino-3-(3-benzylthio)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine
 1-(2(R)-Amino-3-[3-(4-nitrobenzylthio)propyl])-2(S)-butyl-4-(1-naphthoyl)piperazine
 2(S)-Butyl-1-[(4-imidazolyl)ethyl]-4-(1-naphthoyl)piperazine
 2(S)-Butyl-1-[(4-imidazolyl)methyl]-4-(1-naphthoyl)piperazine
 2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl]acetyl-4-(1-naphthoyl)piperazine
 2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl]ethyl-4-(1-naphthoyl)piperazine
 1-(2(R)-Amino-3-hydroxypropyl)-2(S)-butyl-4-(1-naphthoyl)piperazine
 1-(2(R)-Amino-4-hydroxybutyl)-2(S)-butyl-4-(1-naphthoyl)piperazine
 1-(2-Amino-3-(2-benzyloxyphenyl)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine

1-(2-Amino-3-(2-hydroxyphenyl)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine
1-[3-(4-imidazolyl)propyl]-2(S)-butyl-4-(1-naphthoyl)piperazine
2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(1-naphthylmethyl)imidazol-5-ylmethyl]-piperazine
2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(2-naphthylmethyl)imidazol-5-ylmethyl]-piperazine
2(S)-n-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine
2(S)-n-Butyl-1-[1-(4-methoxybenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine
2(S)-n-Butyl-1-[1-(3-methyl-2-butenyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine
2(S)-n-Butyl-1-[1-(4-fluorobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine
2(S)-n-Butyl-1-[1-(4-chlorobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine
1-[1-(4-Bromobenzyl)imidazol-5-ylmethyl]-2(S)-n-butyl-4-(1-naphthoyl)piperazine
1-[1-(4-Bromobenzyl)imidazol-5-ylmethyl]-2(S)-n-butyl-4-(1-naphthoyl)piperazine
2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethylbenzyl)imidazol-5-ylmethyl]-
piperazine
2(S)-n-Butyl-1-[1-(4-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)-piperazine
2(S)-n-Butyl-1-[1-(3-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)-piperazine
1-[1-(4-Phenylbenzyl)imidazol-5-ylmethyl]-2(S)-n-butyl-4-(1-naphthoyl)-piperazine
2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(2-phenylethyl)imidazol-5-ylmethyl]-piperazine
2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethoxy)-imidazol-5-ylmethyl]piperazine
1-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}-2(S)-n-butyl-4-(1-naphthoyl)piperazine
5(S)-n-Butyl-1-(2,3-dimethylphenyl)-4-(4-imidazolylmethyl)-piperazin-2-one
5(S)-n-Butyl-4-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-1-(2,3-
dimethylphenyl)piperazin-2-one
4-[1-(4-Cyanobenzyl)imidazol-5-ylmethyl]-1-(2,3-dimethylphenyl)-5(S)-(2-
methoxyethyl)piperazin-2-one
(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-
(methanesulfonyl)ethyl]-2-piperazinone
(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-
(ethanesulfonyl)ethyl]-2-piperazinone
(R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-
(ethanesulfonyl)methyl]-2-piperazinone
(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[N-ethyl-2-
acetamido]-2-piperazinone
(±)-5-(2-Butynyl)-1-(3-chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-
piperazinone

1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone
 5(S)-Butyl-4-[1-(4-cyanobenzyl-2-methyl)-5-imidazolymethyl]-1-(2,3-dimethylphenyl)-piperazin-2-one
 4-[1-(2-(4-Cyanophenyl)-2-propyl)-5-imidazolymethyl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonylethyl)piperazin-2-one
 5(S)-n-Butyl-4-[1-(4-cyanobenzyl)-5-imidazolymethyl]-1-(2-methylphenyl)piperazin-2-one
 4-[1-(4-Cyanobenzyl)-5-imidazolymethyl]-5(S)-(2-fluoroethyl)-1-(3-chlorophenyl)piperazin-2-one
 4-[3-(4-Cyanobenzyl)pyridin-4-yl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonylethyl)-piperazin-2-one
 4-[5-(4-Cyanobenzyl)-1-imidazolethyl]-1-(3-chlorophenyl)piperazin-2-one
 or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount.

[00199] In certain embodiments, the invention provides a method of treating a subject with a lysosomal storage disease by administering one or more of the following farnesyl transferase inhibitor compounds:

1-{5-[1-(4-Nitrobenzyl)imidazolyl]methyl}-2(S)-butyl-4-(1-naphthoyl)piperazine;
 1-[5-(1-Benzylimidazol)methyl]-2(S)-butyl-4-(1-naphthoyl)piperazine;
 1-(2(R)-Amino-3-(3-benzylthio)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;
 1-(2(R)-Amino-3-[3-(4-nitrobenzylthio)propyl])-2(S)-butyl-4-(1-naphthoyl)piperazine;
 2(S)-n-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;
 2(S)-n-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3dimethylphenyl)piperazin-5-one;
 2(S)-n-Butyl-1-[1-(4-chlorobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;
 1-{[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]acetyl}-2(S)-n-butyl-4-(1-naphthoyl)piperazine;
 1-[1-(4-Cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3-dimethylphenyl)-2(S)-(2-methoxyethyl)piperazin-5-one;
 5(S)-n-Butyl-4-[1-(4-cyanobenzyl)-5-imidazolymethyl]-1-(2-methylphenyl)piperazin-2-one;
 (S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolymethyl]-5-[2-(methanesulfonyl)ethyl]-2-piperazinone;

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)ethyl]-2-piperazinone;

(R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolyl-methyl]-2-piperazinone;

or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount.

[00200] In one embodiment, the compound may be 1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolyl-methyl]-2-piperazinone or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof.

[00201] In another aspect, the invention provides a method of treating a subject with a lysosomal storage disease by administering one or more of the following farnesyl transferase inhibitor compounds:

5(S)-n-Butyl-1-(2,3-dimethylphenyl)-4-(4-imidazolylmethyl)-piperazin-2-one;

5(S)-n-Butyl-4-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-1-(2,3-dimethylphenyl)piperazin-2-one;

4-[1-(4-Cyanobenzyl)imidazol-5-ylmethyl]-1-(2,3-dimethylphenyl)-5(S)-(2-methoxyethyl)piperazin-2-one;

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(methanesulfonyl)ethyl]-2-piperazinone;

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)ethyl]-2-piperazinone;

(R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[N-ethyl-2-acetamido]-2-piperazinone;

(±)-5-(2-Butynyl)-1-(3-chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

5(S)-Butyl-4-[1-(4-cyanobenzyl-2-methyl)-5-imidazolylmethyl]-1-(2,3-dimethylphenyl)-piperazin-2-one;

4-[1-(2-(4-Cyanophenyl)-2-propyl)-5-imidazolylmethyl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonyl)ethyl)piperazin-2-one;

5(S)-n-Butyl-4-[1-(4-cyanobenzyl)-5-imidazolymethyl]-1-(2-methylphenyl)piperazin-2-one;

4-[1-(4-Cyanobenzyl)-5-imidazolymethyl]-5(S)-(2-fluoroethyl)-1-(3-chlorophenyl)piperazin-2-one; or

4-[5-(4-Cyanobenzyl)-1-imidazolethyl]-1-(3-chlorophenyl)piperazin-2-one.

[00202] In certain embodiments, the invention provides a method of treating a subject with a lysosomal storage disease by administering one or more of the following farnesyl transferase inhibitor compounds:

1-(3-Trifluoromethoxyphenyl)-4-[1-(4-cyanobenzyl)imidazolymethyl]-2-piperazinone;

1-(2,5-Dimethylphenyl)-4-[1-(4-cyanobenzyl)imidazolymethyl]-2-piperazinone;

1-(3-Methylphenyl)-4-[1-(4-cyanobenzyl)imidazolymethyl]-2-piperazinone;

1-(3-Iodophenyl)-4-[1-(4-cyanobenzyl)imidazolymethyl]-2-piperazinone;

1-(3-Chlorophenyl)-4-[1-(3-methoxy-4-cyanobenzyl)imidazolymethyl]-2-piperazinone

1-(3-Trifluoromethoxyphenyl)-4-[1-(3-methoxy-4-cyanobenzylimidazo)ylmethyl]-2-piperazinone;

(R)-5-[(Benzyloxy)methyl]-1-(3-chlorophenyl)-4-[1-(4-cyanobenzyl)-imidazolymethyl]-2-piperazinone;

1-(3-Chlorophenyl)-4-[1-(2-fluoro-4-cyanobenzyl)-1H-imidazol-5-ylmethyl]piperazin-2-one;

4-[1-(4-Cyanobenzyl)-1H-imidazol-5-ylmethyl]-1-(3-methylthiophenyl)piperazin-2-one;

4-[1-(4-Cyanobenzyl)-1H-imidazol-5-ylmethyl]-1-(3,5-dichlorophenyl)piperazin-2-one;

1-(3-Chlorophenyl)-4-{[1-(4-cyanophenyl)-1-ethyl]-1H-imidazol-5-ylmethyl}piperazin-2-one;

1-(3-Chloro-4-fluorophenyl)-4-[1-(4-cyanobenzyl)-1H-imidazol-5-ylmethyl]-piperazin-2-one;

4-[1-(4-Cyanobenzyl)-1H-imidazol-5-ylmethyl]-1-(3,5-dimethylphenyl)piperazin-2-one;

(S)-5-Benzyl-4-[3-(4-cyanobenzyl-1-imidazol-5-yl)prop-1-yl]-1-phenyl-2-piperazinone;

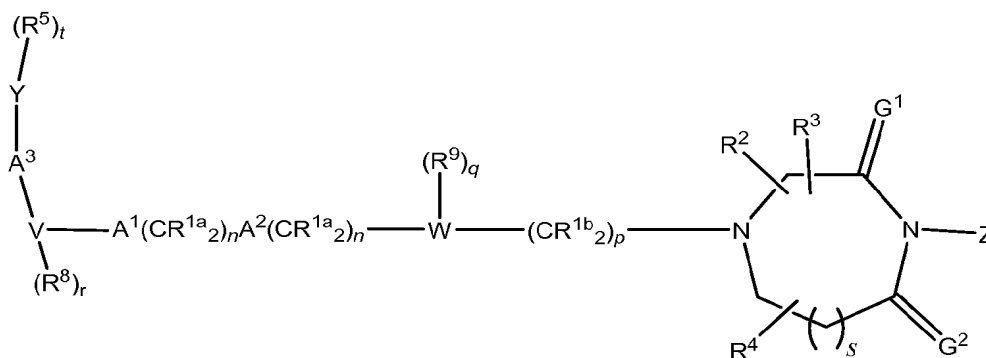
1-(3-Chlorophenyl)-4-[1-(4-nitrobenzyl)-1H-imidazol-5-ylmethyl]piperazin-2-one;

4-[1-(4-Cyanobenzyl)-1H-imidazol-5-ylmethyl]-1-(3,5-difluorophenyl)piperazin-2-one;

or

4-[1-(4-Cyanobenzyl)-1H-imidazol-5-ylmethyl]-1-(3,4-difluorophenyl)piperazin-2-one.

[00203] In certain embodiments, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

wherein:

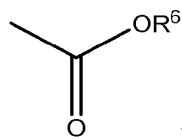
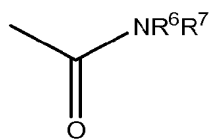
R^{1a} and R^{1b} are independently selected from:

a) hydrogen,

b) unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C₃-C₁₀ cycloalkyl, unsubstituted or substituted C₂-C₈ alkenyl, unsubstituted or substituted C₂-C₈ alkynyl, R¹⁰O—, R¹¹S(O)_m—, R¹⁰C(O)NR¹⁰—, (R¹⁰)₂NC(O)—, (R¹⁰)₂NC(O)NR¹⁰—, CN, NO₂, R¹⁰C(O)—, R¹⁰OC(O)—, —N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰—, or

c) unsubstituted or substituted C₁-C₆ alkyl wherein the substituent on the substituted C₁-C₆ alkyl is selected from unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C₃-C₁₀ cycloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, R¹⁰O—, R¹¹S(O)_m—, R¹⁰C(O)NR¹⁰—, (R¹⁰)₂NC(O)—, (R¹⁰)₂NC(O)NR¹⁰—, CN, R¹⁰OC(O)—, R¹⁰OC(O)—, —N(R¹⁰)₂, and R¹¹OC(O)NR¹⁰—;

R² and R³ are independently selected from: H, unsubstituted or substituted C₁₋₆ alkyl, unsubstituted or substituted C₂₋₈ alkenyl, unsubstituted or substituted C₂₋₈ alkynyl, unsubstituted or substituted aryl, unsubstituted or substituted heterocycle,



wherein the substituted group is substituted

with one or more of:

1) aryl or heterocycle, unsubstituted or substituted with:

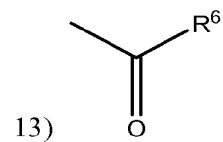
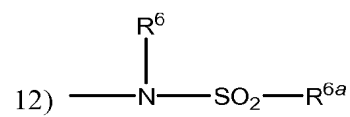
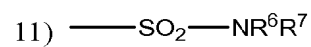
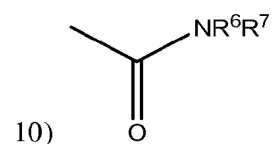
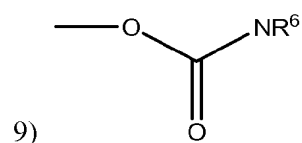
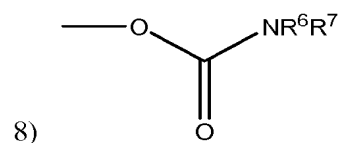
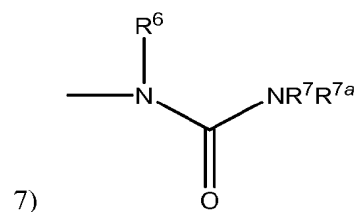
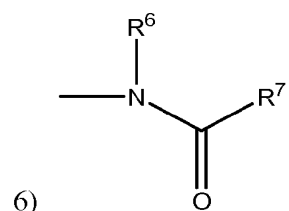
a) C₁₋₆ alkyl,

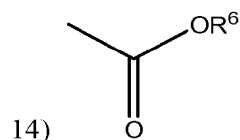
b) (CH₂)_pOR⁶,

c) (CH₂)_pNR⁶R⁷,

d) halogen,

e) CN,

2) C₃₋₆ cycloalkyl,3) OR⁶,4) SR^{6a}, S(O)R^{6a}, SO₂R^{6a},5) -NR⁶R⁷,



15) N₃ or

16) F; or

R² and R³ are attached to the same C atom and are combined to form —(CH₂)_u— wherein one of the carbon atoms is optionally replaced by a moiety selected from: O, S(O)_m, —NC(O)—, and —N(COR¹⁰)—;

R⁴ is selected from H and unsubstituted or substituted C₁-C₆ alkyl;

and any two of R², R³ or R⁴ are optionally attached to the same carbon atom;

R⁵ is independently selected from:

a) hydrogen,

b) unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C₃-C₁₀ cycloalkyl, unsubstituted or substituted C₂-C₈ alkenyl, unsubstituted or substituted C₂-C₈ alkynyl, perfluoroalkyl, halo, R¹⁰O—, unsubstituted or substituted C₁-C₆ alkoxy, R¹¹S(O)_m—, R¹⁰OC(O)NR¹⁰—, (R¹⁰)₂NC(O)—, (R¹⁰)₂NC(O)NR¹⁰—, CN, NO₂, R¹⁰OC(O)—, R¹⁰OC(O)—, —N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰—, and

c) C₁-C₆ alkyl, unsubstituted or substituted by aryl, cyanophenyl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰O—, R¹¹S(O)_m—, R¹⁰C(O)NR¹⁰—, (R¹⁰)₂NC(O)—, (R¹⁰)₂NC(O)NR¹⁰—, CN, R¹⁰C(O)—, R¹⁰OC(O)—, —N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰—;

R⁶, R⁷ and R^{7a} are independently selected from: H, C₁-C₆ alkyl, C₃₋₆ cycloalkyl, heterocycle, aryl, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with:

a) C₁₋₆ alkoxy,

b) C₁-C₂₀ alkyl

c) aryl or heterocycle,

d) halogen,

e) HO,

f) —C(O)R¹¹,

g) —SO₂R¹¹, or

h) N(R¹⁰)₂; or

R^6 and R^7 may be joined in a ring;

R^7 and R^7a may be joined in a ring;

R^{6a} is selected from: C_1 - C_6 alkyl, C_{3-6} cycloalkyl, heterocycle, aryl, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with:

- a) C_{1-4} alkoxy,
- b) C_1 - C_{20} alkyl
- c) aryl or heterocycle,
- d) halogen,
- e) HO,
- f) $—C(O)R^{11}$,
- g) $—SO_2R^{11}$, or
- h) $N(R^{10})_2$;

R^8 is independently selected from:

- a) hydrogen,
- b) unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C_3 - C_{10} cycloalkyl, unsubstituted or substituted C_2 - C_8 alkenyl, unsubstituted or substituted C_2 - C_8 alkynyl, perfluoroalkyl, halo, $R^{10}O—$, unsubstituted or substituted C_1 - C_6 alkoxy, $R^{11}S(O)_m—$, $R^{10}C(O)NR^{10}—$, $(R^{10})_2NC(O)—$, $(R^{10})_2NC(O)NR^{10}—$, CN, NO_2 , $R^{10}C(O)—$, $R^{10}OC(O)—$, $—N(R^{10})_2$, or $R^{11}OC(O)NR^{10}—$, and

- c) C_1 - C_6 alkyl unsubstituted or substituted by aryl, cyanophenyl, heterocycle, C_3 - C_{10} cycloalkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, perfluoroalkyl, halo, $R^{10}O—$, $R^{11}S(O)_m—$, $R^{10}C(O)NR^{10}—$, $(R^{10})_2NC(O)—$, $(R^{10})_2NC(O)NR^{10}—$, CN, $R^{10}C(O)—$, $R^{10}OC(O)—$, $—N(R^{10})_2$, or $R^{11}C(O)NR^{10}—$;

R^9 is selected from:

- a) hydrogen,
- b) unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C_3 - C_{10} cycloalkyl, unsubstituted or substituted C_2 - C_8 alkenyl, unsubstituted or substituted C_2 - C_8 alkynyl, perfluoroalkyl, halo, $R^{10}O—$, $R^{11}S(O)_m—$, $R^{10}C(O)NR^{10}—$, $(R^{10})_2NC(O)—$, $(R^{10})_2NC(O)NR^{10}—$, CN, NO_2 , $R^{10}C(O)—$, $R^{10}OC(O)—$, $—N(R^{10})_2$, or $R^{11}OC(O)NR^{10}—$, and

- c) C_1 - C_6 alkyl unsubstituted or substituted by aryl, heterocycle, C_3 - C_{10} cycloalkyl, perfluoroalkyl, halo, $R^{10}O—$, $R^{11}S(O)_m—$, $R^{10}C(O)NR^{10}—$, $(R^{10})_2NC(O)—$, $(R^{10})_2NC(O)NR^{10}—$, CN, $R^{10}C(O)—$, $R^{10}OC(O)—$, $—N(R^{10})_2$, or $R^{11}OC(O)NR^{10}—$;

R^{10} is independently selected from hydrogen, unsubstituted or substituted C_1 - C_6 alkyl, perfluoroalkyl, unsubstituted or substituted aralkyl, and unsubstituted or substituted aryl;

R^{11} is independently selected from unsubstituted or substituted C_1 - C_6 alkyl and unsubstituted or substituted aryl;

A^1 and A^2 are independently selected from: a bond, $—CH=CH—$, $—C\equiv C—$, $—C(O)—$, $—C(O)NR^{10}—$, $—NR^{10}C(O)—$, O, $—N(R^{10})—$, $—S(O)_2N(R^{10})—$, $—N(R^{10})S(O)_2—$, or $S(O)_m$;

A^3 is selected from $—C(O)—$, $—C(R^{1a})_2—$, O, $—N(R^{10})—$ and $S(O)_m$;

G^1 or G^2 is selected from H_2 or O, provided that if G^1 is O then G^2 is H_2 and if G^2 is O, then G^1 is H_2 ;

V is selected from:

- a) heterocycle, and
- b) aryl,

W is a heterocycle;

Y is heteroaryl;

Z is a unsubstituted or substituted group selected from aryl, heteroaryl, arylmethyl, heteroaryl methyl, arylsulfonyl, heteroarylsulfonyl, wherein the substituted group is substituted with one or more of the following:

1. C_1 - C_6 alkyl, unsubstituted or substituted with:

- a) C_{1-6} alkoxy,
- b) NR^6R^7 ,
- c) C_{3-6} cycloalkyl,
- d) aryl or heterocycle,
- e) HO,
- f) $—S(O)_mR^{6a}$, or
- g) $—C(O)NR^6R^7$,

2. unsubstituted or substituted aryl or unsubstituted or substituted heterocycle,

3. halogen,

4. OR^6 ,

5. NR^6R^7 ,

6. CN,

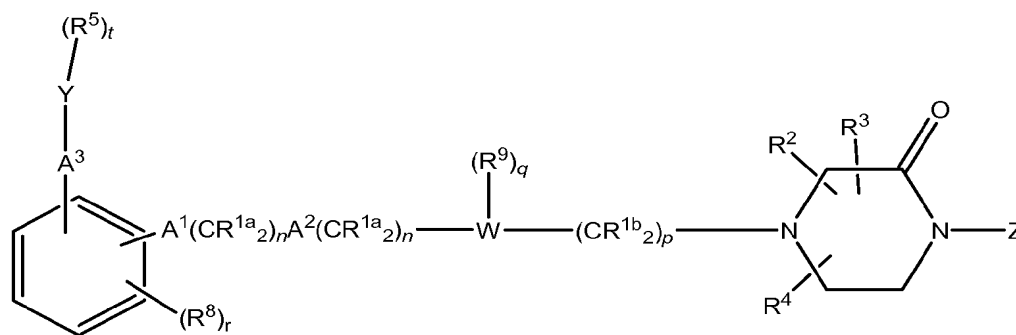
7. NO_2 ,

8. CF_3 ,

9. $—S(O)_mR^{6a}$,

10. $-\text{C}(\text{O})\text{NR}^6\text{R}^7$,
 11. $-\text{OCF}_3$,
 12. unsubstituted or substituted C_{1-6} alkoxy,
 13. $\text{C}_2\text{-C}_8$ alkenyl,
 14. $\text{C}_2\text{-C}_8$ alkynyl, or
 15. $\text{C}_3\text{-C}_{10}$ cycloalkyl;
- m is 0, 1 or 2;
 n is 0, 1, 2, 3 or 4;
 p is 0, 1, 2, 3 or 4;
 q is 0, 1 or 2;
 r is 0 to 5;
 s is 0 or 1;
 t is 0 to 5;
 u is 4 or 5; and
 x is 0, 1, 2, 3 or 4.

[00204] In another aspect, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

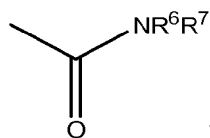
wherein:

R^{1a} and R^{1b} are independently selected from:

- a) hydrogen,
- b) unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{R}^{10}\text{O}-$, $-\text{N}(\text{R}^{10})_2$, or, $\text{C}_2\text{-C}_8$ alkenyl, or
- c) unsubstituted or substituted $\text{C}_1\text{-C}_6$ alkyl wherein the substituent on the substituted

C₁-C₆ alkyl is selected from unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C₃-C₁₀ cycloalkyl, C₂-C₈ alkenyl, R¹⁰O—, or —N(R¹⁰)₂;

R² and R³ are independently selected from: H, unsubstituted or substituted C₁₋₆



wherein the substituted group is substituted with one or more of:

1) aryl or heterocycle, unsubstituted or substituted with:

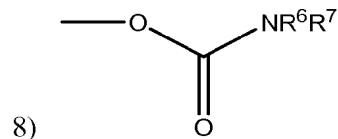
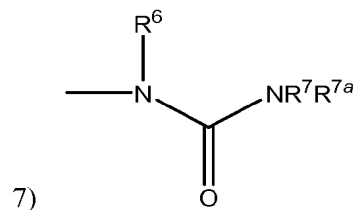
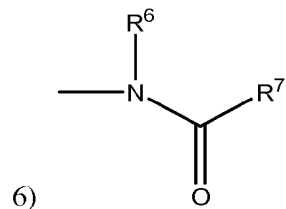
- a) C₁-C₆ alkyl,
- b) (CH₂)_pOR⁶,
- c) (CH₂)_pNR⁶R⁷,
- d) halogen,
- e) CN;

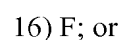
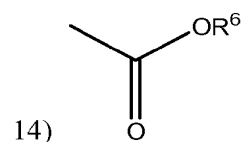
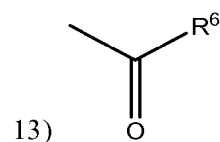
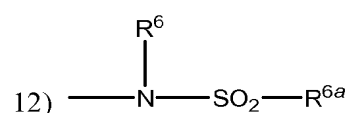
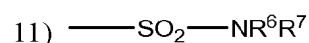
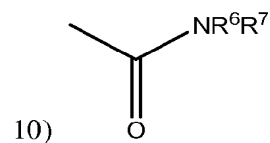
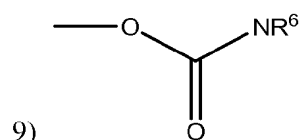
2. C₃₋₆ cycloalkyl;

3. OR⁶;

4. SR^{6a}, S(O)R^{6a}, SO₂R^{6a},

5) -NR⁶R⁷,





R² and R³ are attached to the same C atom and are combined to form $-(CH_2)_u-$ wherein one of the carbon atoms is optionally replaced by a moiety selected from: O, S(O)_m, $-NC(O)-$, and $-N(COR^{10})-$;

R⁴ is selected from H and unsubstituted or substituted C₁-C₆ alkyl;

and any two of R², R³ or R⁴ are optionally attached to the same carbon atom;

R⁵ is independently selected from:

a) hydrogen,

b) unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C₃-C₁₀ cycloalkyl, unsubstituted or substituted C₂-C₈ alkenyl, unsubstituted or substituted C₂-C₈ alkynyl, perfluoroalkyl, halo, R¹⁰O—, unsubstituted or substituted C₁-C₆ alkoxy, R¹ S(O)_m—, R¹⁰C(O)NR¹⁰—, (R¹⁰)₂NC(O)—, (R¹⁰)₂NC(O)NR¹⁰—, CN, NO₂, R¹⁰C(O)—, R¹⁰OC(O)—, $-N(R^{10})_2$, or R¹¹OC(O)NR¹⁰—, and

c) C₁-C₆ alkyl unsubstituted or substituted by aryl, cyanophenyl, heterocycle, C₃-C₁₀ cycloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰O—, R¹¹S(O)_m—, R¹⁰C(O)NR¹⁰—, (R¹⁰)₂NC(O)—, (R¹⁰)₂NC(O)NR¹⁰—, CN, R¹⁰C(O)—, R¹⁰OC(O)—, —N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰—;

R⁶, R⁷ and R^{7a} are independently selected from: H, C₁-C₆ alkyl, C₃₋₆ cycloalkyl, heterocycle, aryl, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with:

- a) C₁₋₆ alkoxy,
- b) C₁-C₂₀ alkyl
- c) aryl or heterocycle,
- d) halogen,
- e) HO,
- f) —C(O)R¹¹,
- g) —SO₂R¹¹, or
- h) N(R¹⁰)₂; or

R⁶ and R⁷ may be joined in a ring;

R⁷ and R^{7a} may be joined in a ring;

R^{6a} is selected from: C₁-C₆ alkyl, C₃₋₆ cycloalkyl, heterocycle, aryl, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with:

- a) C₁₋₆ alkoxy,
- b) C₁-C₂₀ alkyl
- c) aryl or heterocycle,
- d) halogen,
- e) HO,
- f) —C(O)R¹¹,
- g) —SO₂R¹¹, or
- h) N(R¹⁰)₂; or

R⁸ is independently selected from:

- a) hydrogen,
- b) unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C₃-C₁₀ cycloalkyl, unsubstituted or substituted C₂-C₈ alkenyl, unsubstituted or substituted C₂-C₈ alkynyl, perfluoroalkyl, halo, R¹⁰O—, unsubstituted or substituted C₁-C₆ alkoxy, R¹¹S(O)_m—, R¹⁰C(O)NR¹⁰—, (R¹⁰)₂NC(O)—, (R¹⁰)₂NC(O)NR¹⁰, CN, NO₂, R¹⁰C(O)—, R¹⁰OC(O)—, —N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰—, and

- c) C₁-C₆ alkyl unsubstituted or substituted by aryl, cyanophenyl, heterocycle, C₃-C₁₀

cycloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, perfluoroalkyl, F, Cl, Br, R¹⁰O—, R¹¹S(O)_m—, R¹⁰C(O)NR¹⁰—, (R¹⁰)₂NC(O)—, (R¹⁰)₂NC(O)NR¹⁰—, CN, R¹⁰C(O)—, R¹⁰OC(O)—, —N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰—;

R⁹ is selected from:

- a) hydrogen,
- b) unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C₃-C₁₀ cycloalkyl, unsubstituted or substituted C₂-C₈ alkenyl, unsubstituted or substituted C₂-C₈ alkynyl, perfluoroalkyl, halo, R¹⁰O—, R¹¹S(O)_m—, R¹⁰C(O)NR¹⁰—, (R¹⁰)₂NC(O)—, (R¹⁰)₂NC(O)NR¹⁰—, R¹⁰2N—C(NR¹⁰)—, CN, NO₂, R¹⁰C(O)—, R¹⁰OC(O)—, N₃, —N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰—, and
- c) C₁-C₆ alkyl unsubstituted or substituted by aryl, heterocycle, C₃-C₁₀ cycloalkyl, perfluoroalkyl, halo, R¹⁰O—, R¹¹S(O)_m—, R¹⁰C(O)NR¹⁰—, (R¹⁰)₂NC(O)—, (R¹⁰)₂NC(O)NR¹⁰—, CN, R¹⁰C(O)—, R¹⁰OC(O)—, —N(R¹⁰)₂, or R¹¹OC(O)NR¹⁰—;

R¹⁰ is independently selected from hydrogen, unsubstituted or substituted C₁-C₆ alkyl, perfluoroalkyl, unsubstituted or substituted aralkyl, and unsubstituted or substituted aryl;

R¹¹ is independently selected from unsubstituted or substituted C₁-C₆ alkyl and unsubstituted or substituted aryl;

A¹ and A² are independently selected from: a bond, —CH=CH—, —C≡C—, —C(O)—, —C(O)NR¹⁰—, —NR¹⁰C(O)—, O, —N(R¹⁰)—, —S(O)₂N(R¹⁰)—, —N(R¹⁰)S(O)₂—, or S(O)_m;

A³ is selected from —C(O)—, —C(R^{1a})₂—, O, —N(R¹⁰)— and S(O)_m;

W is a heterocycle selected from imidazolyl, pyridyl, thiazolyl, indolyl, quinolinyl, isoquinolinyl and thienyl;

Y is heteroaryl;

Z is a unsubstituted or substituted group selected from aryl, heteroaryl, arylmethyl, heteroarylmethyl, arylsulfonyl, heteroarylsulfonyl, wherein the substituted group is substituted with one or more of the following:

1. C₁-C₆ alkyl, unsubstituted or substituted with:

- a) C₁₋₆ alkoxy,
- b) NR⁶R⁷,
- c) C₃₋₆ cycloalkyl,
- d) aryl or heterocycle,
- e) HO,
- f) —S(O)_mR^{6a}, or
- g) —C(O)NR⁶R⁷,

2. unsubstituted or substituted aryl or unsubstituted or substituted heterocycle,
3. halogen,
4. OR^6 ,
5. NR^6R^7 ,
6. CN ,
7. NO_2 ,
8. CF_3 ;
9. $-\text{S}(\text{O})_m\text{R}^{6a}$,
10. $-\text{C}(\text{O})\text{NR}^6\text{R}^7$,
11. $\text{C}_3\text{-C}_6$ cycloalkyl,
12. $-\text{OCF}_3$, or
13. unsubstituted or substituted C_{1-6} alkoxy;

m is 0, 1 or 2;

n is 0, 1, 2, 3 or 4;

p is 0, 1, 2, 3 or 4;

q is 0, 1 or 2;

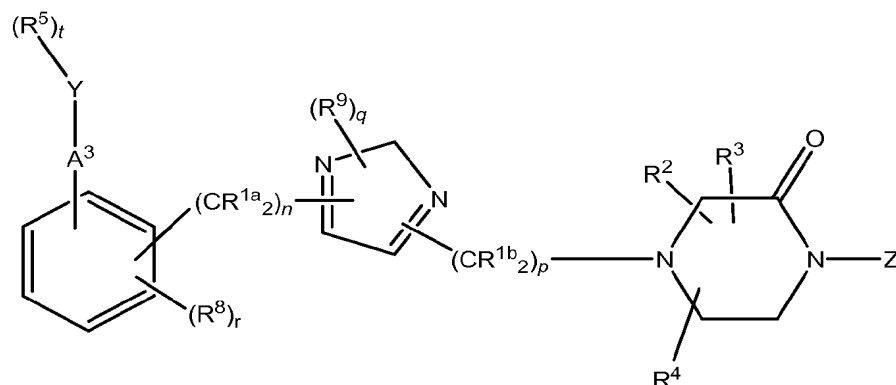
r is 0 to 5;

t is 0 to 5;

u is 4 or 5; and

x is 0, 1, 2, 3 or 4.

[00205] In another aspect, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the formula:

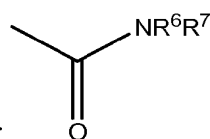


or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

wherein: R^{1a} and R^{1b} are independently selected from:

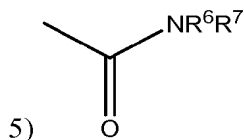
- a) hydrogen,
- b) unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C_3 - C_{10} cycloalkyl, unsubstituted or substituted C_2 - C_8 alkenyl, $R^{10}O$ —, or — $N(R^{10})_2$, or
- c) unsubstituted or substituted C_1 - C_6 alkyl wherein the substituent on the substituted C_1 - C_6 alkyl is selected from unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C_3 - C_{10} cycloalkyl, C_2 - C_8 alkenyl, $R^{10}O$ —, or — $N(R^{10})_2$;

R^2 is H, unsubstituted or substituted C_{1-6} alkyl, or group is substituted with one or more of:



wherein the substituted

- 1) aryl,
- 2) heterocycle,
- 3) OR^6 ,
- 4) SR^{6a} , SO_2R^{6a} , or



R^3 and R^4 are independently selected from H and unsubstituted or substituted C_1 - C_6 alkyl; and any two of R^2 , R^3 or R^4 are optionally attached to the same carbon atom;

R^5 is independently selected from:

- a) hydrogen,
- b) unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C_3 - C_{10} cycloalkyl, unsubstituted or substituted C_2 - C_8 alkenyl, unsubstituted or substituted C_2 - C_8 alkynyl, perfluoroalkyl, halo, $R^{10}O$ —, unsubstituted or substituted C_1 - C_6 alkoxy, $R^{11}S(O)_m$ —, $R^{10}C(O)NR^{10}$ —, $(R^{10})_2NC(O)$ —, $(R^{10})_2NC(O)NR^{10}$ —, CN, NO_2 , $R^{10}C(O)$ —, $R^{10}OC(O)$ —, — $N(R^{10})_2$, or $R^{11}OC(O)NR^{10}$ —, and

c) C_1 - C_6 alkyl unsubstituted or substituted by aryl, cyanophenyl, heterocycle, C_3 - C_{10} cycloalkyl, perfluoroalkyl, F, Cl, Br, $R^{10}O$ —, $R^{11}S(O)_m$ —, $R^{10}C(O)NR^{10}$ —, $(R^{10})_2NC(O)$ —, $(R^{10})_2NC(O)NR^{10}$ —, CN, $R^{10}C(O)$ —, $R^{10}OC(O)$ —, — $N(R^{10})_2$, or $R^{11}OC(O)NR^{10}$ —;

R^6 and R^7 are independently selected from: H, C_1 - C_6 alkyl, C_{3-6} cycloalkyl, heterocycle, aryl, unsubstituted or substituted with:

- a) C_{1-6} alkoxy,
- b) C_1 - C_{20} alkyl
- c) aryl or heterocycle,
- d) halogen, or
- e) HO;

R^6 and R^7 may be joined in a ring;

R^{6a} is selected from: C_1 - C_6 alkyl, C_{3-6} cycloalkyl, heterocycle, aryl, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, unsubstituted or substituted with: a) C_{1-6} alkoxy,

- b) C_1 - C_{20} alkyl
- c) aryl or heterocycle,
- d) halogen, or
- e) HO;

R^8 is independently selected from:

- a) hydrogen,
- b) unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C_3 - C_{10} cycloalkyl, unsubstituted or substituted C_2 - C_8 alkenyl, unsubstituted or substituted C_2 - C_8 alkynyl, perfluoroalkyl, halo, $R^{10}O$ —, unsubstituted or substituted C_1 - C_6 alkoxy, $R^{11}S(O)_m$ —, $R^{10}C(O)NR^{10}$ —, $(R^{10})_2NC(O)$ —, $(R^{10})_2NC(O)NR^{10}$ —, CN, NO_2 , $R^{10}C(O)$ —, $R^{10}OC(O)$ —, $—N(R^{10})_2$, or $R^{11}OC(O)NR^{10}$ —, and

- c) C_1 - C_6 alkyl unsubstituted or substituted by aryl, cyanophenyl, heterocycle, C_3 - C_{10} cycloalkyl, perfluoroalkyl, halo, $R^{10}O$ —, $R^{11}S(O)_m$ —, $R^{10}C(O)NR^{10}$ —, $(R^{10})_2NC(O)$ —, $(R^{10})_2NC(O)NR^{10}$ —, CN, $R^{10}C(O)$ —, $R^{10}OC(O)$ —, $—N(R^{10})_2$, or $R^{10}OC(O)NR^{10}$ —;

R^9 is selected from:

- a) hydrogen,
- b) unsubstituted or substituted aryl, unsubstituted or substituted heterocycle, unsubstituted or substituted C_3 - C_{10} cycloalkyl, unsubstituted or substituted C_2 - C_8 alkenyl, unsubstituted or substituted C_2 - C_8 alkynyl, perfluoroalkyl, halo, $R^{10}O$ —, $R^{11}S(O)_m$ —, $R^{10}C(O)NR^{10}$ —, $(R^{10})_2NC(O)$ —, $(R^{10})_2NC(O)NR^{10}$ —, CN, NO_2 , $R^{10}C(O)$ —, $R^{10}OC(O)$ —, $—N(R^{10})_2$, or $R^{11}OC(O)NR^{10}$ —, and

- c) C_1 - C_6 alkyl unsubstituted or substituted by aryl, heterocycle, C_3 - C_{10} cycloalkyl, perfluoroalkyl, halo, $R^{10}O$ —, $R^{11}S(O)_m$ —, $R^{10}C(O)NR^{10}$ —, $(R^{10})_2NC(O)$ —, $(R^{10})_2NC(O)NR^{10}$ —, CN, $R^{10}C(O)$ —, $R^{10}OC(O)$ —, $—N(R^{10})_2$, or $R^{11}OC(O)NR^{10}$ —;

R¹⁰ is independently selected from hydrogen, unsubstituted or substituted C₁-C₆ alkyl, perfluoroalkyl, unsubstituted or substituted aralkyl, and unsubstituted or substituted aryl;

R¹¹ is independently selected from unsubstituted or substituted C₁-C₆ alkyl and unsubstituted or substituted aryl;

A³ is selected from —C(O)—, —C(R^{1a})₂—, O, —N(R¹⁰)— and S(O)_m;

Y is heteroaryl;

Z is a unsubstituted or substituted group selected from aryl, heteroaryl, arylmethyl, heteroarylmethyl, wherein the substituted group is substituted with one or more of the following:

1. C₁-C₆ alkyl, unsubstituted or substituted with: a) C₁₋₆ alkoxy, b) NR^{6R7}, c) C₃₋₆ cycloalkyl, d) aryl or heterocycle, e) HO, f) —S(O)_mR^{6a}, or g) —C(O)NR^{6R7}, 2. unsubstituted or substituted aryl or unsubstituted or substituted heterocycle, 3. halogen, 4. OR⁶, 5. NR^{6R7}, 6. CN, 7. NO₂, 8. CF₃; 9. —S(O)_mR^{6a}, 10. —C(O)NR^{6R7}, 11. C₃-C₆ cycloalkyl, 12. —OCF₃, or 13. unsubstituted or substituted C₁₋₆ alkoxy;

m is 0, 1 or 2; n is 0, 1, 2, 3 or 4; p is 0, 1, 2, 3 or 4; q is 0, 1 or 2; r is 0 to 5; t is 0 to 5; and u is 4 or 5.

[00206] In certain embodiments, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the list comprising of: (3-chlorophenyl)-4-[1-(3-(3-pyridyloxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone; and 1-(2-(n-Butyloxy)phenyl)-4-[1-(3-((6-methyl-2-pyridyl)oxy)-4-cyanobenzyl)-2-methyl-5-imidazolymethyl]-2-piperazinone; or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount.

[00207] In certain embodiments, the invention provides a method of treating a subject with a lysosomal storage disease by administering one or more of the following farnesyl transferase inhibitor compounds: 1-(3-chlorophenyl)-4-[1-(3-((2-chlorophenyl)oxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone; 1-(3-chlorophenyl)-4-[1-(3-((3-chlorophenyl)oxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone; 1-(3-chlorophenyl)-4-[1-(3-((4-chlorophenyl)oxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone; 1-(3-chlorophenyl)-4-[1-(3-((4-biphenyl)oxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone; 1-(3-chlorophenyl)-4-[1-(3-((3-(2-hydroxy-1-ethoxy)phenyl)oxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone; 1-(3-chlorophenyl)-4-[1-(3-((4-(benzyloxy)phenyl)oxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone; and 1-(2-(n-

Butyloxy)phenyl)-4-[1-(3-((3-(2-hydroxy-1-ethoxy)phenyl)oxy)-4-cyanobenzyl)-2-methyl-5-imidazolymethyl]-2-piperazinone, or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount.

[00208] In one embodiment, the compound may be 1-(3-chlorophenyl)-4-[1-(3-((2-chlorophenyl)oxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone. In another embodiment, the compound may be 1-(3-chlorophenyl)-4-[1-(3-((3-chlorophenyl)oxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone. In another embodiment, the compound may be 1-(3-chlorophenyl)-4-[1-(3-((4-chlorophenyl)oxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone. In another embodiment, the compound may be 1-(3-chlorophenyl)-4-[1-(3-((4-biphenyl)oxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone. In another embodiment, the compound may be 1-(3-chlorophenyl)-4-[1-(3-((3-(2-hydroxy-1-ethoxy)phenyl)oxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone. In another embodiment, the compound may be 1-(3-chlorophenyl)-4-[1-(3-((4-(benzyloxy)phenyl)oxy)-4-cyanobenzyl)-5-imidazolymethyl]-2-piperazinone. In another embodiment, the compound may be 1-(2-(n-Butyloxy)phenyl)-4-[1-(3-((3-(2-hydroxy-1-ethoxy)phenyl)oxy)-4-cyanobenzyl)-2-methyl-5-imidazolymethyl]-2-piperazinone.

[00209] In another aspect, the invention provides a method of treating a subject with a lysosomal storage disease by administering one or more of the following farnesyl transferase inhibitor compounds: 2(S)-Butyl-1-(2,3-diaminoprop-1-yl)-1-(1-naphthoyl)piperazine; 1-(3-Amino-2-(2-naphthylmethylamino)prop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine; 2(S)-Butyl-1-{5-[1-(2-naphthylmethyl)]-4,5-dihydroimidazol}methyl-4-(1-naphthoyl)piperazine; 1-[5-(1-Benzylimidazol)methyl]-2(S)-butyl-4-(1-naphthoyl)piperazine; 1-{(5-[1-(4-nitrobenzyl)]imidazolymethyl)-2(S)-butyl-4-(1-naphthoyl)piperazine; 1-(3-Acetamidomethylthio-2(R)-aminoprop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine; 2(S)-Butyl-1-[2-(1-imidazolyl)ethyl]sulfonyl-4-(1-naphthoyl)piperazine; 2(R)-Butyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine; 2(S)-Butyl-4-(1-naphthoyl)-1-(3-pyridylmethyl)piperazine; 1-2(S)-butyl-(2(R)-(4-nitrobenzyl)amino-3-hydroxypropyl)-4-(1-naphthoyl)piperazine; 1-(2(R)-Amino-3-hydroxyheptadecyl)-2(S)-butyl-4-(1-naphthoyl)piperazine; 2(S)-Benzyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine; 1-(2(R)-Amino-3-(3-benzylthio)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine; 1-(2(R)-Amino-3-[3-(4-nitrobenzylthio)propyl])-2(S)-butyl-4-(1-naphthoyl)piperazine; 2(S)-Butyl-1-[(4-imidazolyl)ethyl]-4-(1-naphthoyl)piperazine; 2(S)-Butyl-1-[(4-imidazolyl)methyl]-4-(1-naphthoyl)piperazine; 2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl]acetyl-4-(1-naphthoyl)piperazine; 2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl]ethyl-4-(1-

naphthoyl)piperazine; 1-(2(R)-Amino-3-hydroxypropyl)-2(S)-butyl-4-(1-naphthoyl)piperazine; 1-(2(R)-Amino-4-hydroxybutyl)-2(S)-butyl-4-(1-naphthoyl)piperazine; 1-(2-Amino-3-(2-benzoyloxyphenyl)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine; 1-(2-Amino-3-(2-hydroxyphenyl)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine; 1-[3-(4-imidazolyl)propyl]-2(S)-butyl-4-(1-naphthoyl)-piperazine; 2(S)-n-Butyl-4-(2,3-dimethylphenyl)-1-(4-imidazolylmethyl)-piperazin-5-one; 2(S)-n-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3-dimethylphenyl)piperazin-5-one; 1-[1-(4-Cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3-dimethylphenyl)-2(S)-(2-methoxyethyl)piperazin-5-one; 2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(1-naphthylmethyl)imidazol-5-ylmethyl]-piperazine; 2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(2-naphthylmethyl)imidazol-5-ylmethyl]-piperazine; 2(S)-n-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine; 2(S)-n-Butyl-1-[1-(4-methoxybenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine; 2(S)-n-Butyl-1-[1-(3-methyl-2-butenyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine; 2(S)-n-Butyl-1-[1-(4-fluorobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine; 2(S)-n-Butyl-1-[1-(4-chlorobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine; 1-[1-(4-Bromobenzyl)imidazol-5-ylmethyl]-2(S)-n-butyl-4-(1-naphthoyl)piperazine; 2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethylbenzyl)imidazol-5-ylmethyl]-piperazine; 2(S)-n-Butyl-1-[1-(4-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)-piperazine; 2(S)-n-Butyl-1-[1-(3-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)-piperazine; 1-[1-(4-Phenylbenzyl)imidazol-5-ylmethyl]-2(S)-n-butyl-4-(1-naphthoyl)-piperazine; 2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(2-phenylethyl)imidazol-5-ylmethyl]-piperazine; 2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethoxy)imidazol-5-ylmethyl]piperazine; 1-1 [1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]-2(S)-n-butyl-4-(1-naphthoyl)piperazine; (S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(methanesulfonyl)ethyl]-2-piperazinone; (S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)ethyl]-2-piperazinone; (R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone; (S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[N-ethyl-2-acetamido]-2-piperazinone; (±)-5-(2-Butynyl)-1-(3-chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone; 1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone; 5(S)-Butyl-4-[1-(4-cyanobenzyl-2-methyl)-5-imidazolylmethyl]-1-(2,3-dimethylphenyl)-piperazin-2-one; 4-[1-(2-(4-Cyanophenyl)-2-propyl)-5-imidazolylmethyl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonyl)ethyl)piperazin-2-one; 5(S)-n-Butyl-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]—(2-methylphenyl)piperazin-2-

one; 4-[1-(4-Cyanobenzyl)-5-imidazolylmethyl]-5(S)-(2-fluoroethyl)-1-(3-chlorophenyl)piperazin-2-one; 4-[3-(4-Cyanobenzyl)pyridin-4-yl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonyl)ethylpiperazin-2-one; 4-[5-(4-Cyanobenzyl)-1-imidazolylethyl]-1-(3-chlorophenyl)piperazin-2-one; 4-{3-[4-(2-Oxo-2-H-pyridin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile; 4-{3-[4-(3-Methyl-2-oxo-2-H-pyridin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile; 4-{3-[4-(2-Oxo-piperidin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile; 4-{3-[3-Methyl-4-(2-oxopiperidin-1-yl)-benzyl]-3-H-imidazol-4-ylmethyl}-benzonitrile; (4-{3-[4-(2-Oxo-pyrrolidin-1-yl)-benzyl]-3H-imidazol-4-ylmethyl}-benzonitrile; 4-13-[4-(3-Methyl-2-oxo-2-H-pyrazin-1-yl)-benzyl]-3-H-imidazol-4-ylmethyl}-benzonitrile; 4-{3-[2-Methoxy-4-(2-oxo-2-H-pyridin-1-yl)-benzyl]-3-H-imidazol-4-ylmethyl}-benzonitrile; 4-{1-[4-(5-Chloro-2-oxo-2H-pyridin-1-yl)-benzyl]-1H-pyrrol-2-ylmethyl}-benzonitrile; 4-[1-(2-Oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile; 4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile; 4-[3-(2-Oxo-1-phenyl-1,2-dihydropyridin-4-ylmethyl)-3H-imidazol-4-ylmethyl]benzonitrile; 4-{3-[1-(3-Chloro-phenyl)-2-oxo-1,2-dihydropyridin-4-ylmethyl]-3H-imidazol-4-ylmethyl}benzonitrile; 19,20-Dihydro-19-oxo-5H,17H-18,21-ethano-6,10:12,16-dimetheno-22H-imidazo[3,4-h][1,8,11,14]oxatriazacycloeicosine-9-carbonitrile; 19-Chloro-22,23-dihydro-22-oxo-5H-21,24-ethano-6,10-metheno-25H-dibenzo[b,e]imidazo[4,3-l][1,4,7,10,13]dioxatriazacyclononadecine-9-carbonitrile; 22,23-Dihydro-22-oxo-5H-21,24-ethano-6,10-metheno-25H-dibenzo[b,e]imidazo[4,3-l][1,4,7,10,13]dioxatriazacyclononadecine-9-carbonitrile; 20-Chloro-23,24-dihydro-23-oxo-5H-22',25-ethano-6,10:12,16-dimetheno-12H,26H-benzo[b]imidazo[4,3-i][1,17,4,7,10]dioxatriazacyclohemicosine-9-carbonitrile; (S)-20-Chloro-23,24-dihydro-27-[2-(methylsulfonyl)ethyl]-23-oxo-5H-22,25-ethano-6,10:12,16-dimetheno-12H,26H-benzo[b]imidazo[4,3-i][1,17,4,7,10]dioxatriazacyclohemicosine-9-carbonitrile; (±)-19,20-Dihydro-19-oxo-5H-18,21-ethano-12,14-etheno-6,10-metheno-22H-benzo[d]imidazo[4,3-k][1,6,9,12]oxatriazacyclooctadecine-9-carbonitrile; (+)-19,20-Dihydro-19-oxo-5H-18,21-ethano-12,14-etheno-6,10-metheno-22H-benzo[d]imidazo[4,3-k][1,6,9,12]oxatriazacyclooctadecine-9-carbonitrile; (-)-19,20-Dihydro-19-oxo-5H-18,21-ethano-12,14-etheno-6,10-metheno-22H-benzo[d]imidazo[4,3-k][1,6,9,12]oxatriazacyclooctadecine-9-carbonitrile; 5H,17H,20H-18,21-Ethano-6,10:12,16-dimetheno-22H-imidazo[3,4-h][1,8,11,14]oxatriazacycloeicosin-20-one; (±)-19,20-Dihydro-3-methyl-19-oxo-5H-18,21-ethano-12,14-etheno-6,10-metheno-22H-benzo[d]imidazo[4,3-k][1,6,9,12]oxatriazacyclooctadecine-9-carbonitrile; (+) or (-)-19,20-Dihydro-3-methyl-19-

oxo-5H-18,21-ethano-12,14-etheno-6,10-metheno-22H-benzo[d]imidazo[4,3-k][1,6,9,12]oxatriazacyclooctadecine-9-carbonitrile; (Enantiomer A) (–) or (+)-19,20-Dihydro-3-methyl-19-oxo-5H-18,21-ethano-12,14-etheno-6,10-metheno-22H-benzo[d]imidazo[4,3-k][1,6,9,12]oxatriazacyclooctadecine-9-carbonitrile; (Enantiomer B) (±)-19,20-Dihydro-19,22-dioxo-5H-18,21-ethano-12,14-etheno-6,10-metheno-22H-benzo[d]imidazo[4,3-k][1,6,9,12]oxatriazacyclooctadecine-9-carbonitrile; 325 18,19-dihydro-19-oxo-5H, 17H-6, 10:12, 16-dimetheno-1H-imidazo[4,3-c][1,11,4]dioxazacyclononadecine-9-carbonitrile; 17,18-dihydro-18-oxo-5H-6,10:12,16-dimetheno-12H,20H-imidazo[4,3-c][1,11,4]dioxazacyclooctadecine-9-carbonitrile; (±)-17,18,19,20-tetrahydro-19-phenyl-5H-6,10:12,16-dimetheno-21H-imidazo[3,4-h][1,8,11]oxadiazacyclononadecine-9-carbonitrile; 21,22-dihydro-5H-6,10:12,16-dimetheno-23H-benzo[g]imidazo[4,3-1][1,8,11]oxadiazacyclononadecine-9-carbonitrile; 22,23-dihydro-23-oxo-5H,21H-6,10:12,16-dimetheno-24H-benzo g]imidazo[4,3-m][1,8,12]oxadiazacosine-9-carbonitrile; 22,23-dihydro-5H,21H-6,10:12,16-dimetheno-24H-benzo[g]imidazo[4,3-m][1,8,11]oxadiazacosine-9-carbonitrile; 1-(3-trifluoromethoxyphenyl)-4-[1-(4-cyano-3-methoxybenzyl)-5-imidazolyl methyl]-2-piperazinone; or a pharmaceutically acceptable salt, stereoisomer or optical isomer thereof. Specific examples of a farnesyl-protein transferase inhibitor are 1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone; (R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone; 4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile; and 1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzene; (±)-19,20-Dihydro-19-oxo-5H-18,21-ethano-12, 14-etheno-6,10-metheno-22H-benzo[d]imidazo[4,3-k][1,6,9,12]oxatriaza-cyclooctadecine-9-carbonitrile; 1-(3-trifluoromethoxyphenyl)-4-[1-(4-cyano-3-methoxybenzyl)-5-imidazolyl methyl]-2-piperazinone; 3-(biphenyl-4-ylmethoxy)-4-imidazol-1-ylmethyl-benzonitrile; 3-(biphenyl-4-yl-2-ethoxy)-4-imidazol-1-ylmethylbenzonitrile; 3-(biphenyl-3-ylmethoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(biphenyl-4-ylmethoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(biphenyl-4-yl-2-ethoxy)-4-imidazol-1-ylmethyl-benzonitrile; 1-tert-butoxycarbonyl-4-(3-chlorophenyl)-2(S)-[2-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)ethyl]piperazine; 2-(3-chlorophenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(4-chlorophenyl-2-ethoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3-chlorophenyl-2-ethoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(phenyl-2-ethoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3-chlorobenzoyloxy)-4-imidazol-1-ylmethyl-

benzonitrile; 2-(4-chlorobenzyloxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2,4-dichlorobenzyloxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(benzyloxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(biphenyl-2-ylmethoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(phenyl-4-butoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(phenyl-3-propoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(biphenyl-4-yl-2-ethoxy)-4-(1,2,4-triazol-1-yl)methyl-benzonitrile; 2-(biphenyl-4-yl-2-ethoxy)-4-(2-methyl-imidazol-1-yl)methyl-benzonitrile; 2-(biphenyl-4-yl-2-ethoxy)-4-benzimidazol-1-yl)methyl-benzonitrile; 4-imidazol-1-ylmethyl-2-(naphthalen-2-yloxy)-benzonitrile; 2-(3-cyanophenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3-bromophenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(biphen-3-yloxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(biphen-4-yloxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3-acetylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2-acetylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3-trifluoromethylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3-methylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2-methylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(4-methylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3-methoxyphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2-methoxyphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(4-methoxyphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3,5-dimethylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3,4-dimethylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3,5-dimethoxyphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(1-naphthylloxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2,4-dichlorophenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3-fluorophenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3-tert-butylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-[3-(N,N-diethylamino)phenoxy]-4-imidazol-1-ylmethyl-benzonitrile; 2-(3-n-propylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2,3-dimethoxyphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2,3-dimethylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3,4-dimethoxyphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2,5-dimethoxyphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3,4-dichlorophenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2,4-dimethylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(4-chloro-2-methylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(5-chloro-2-methylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2-chloro-4,5-dimethylphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(5-hydroxymethyl-2-methoxyphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 4-imidazol-1-ylmethyl-2-(3-phenylamino-phenoxy)-benzonitrile; 4-imidazol-1-ylmethyl-2-[3-(2-methylphenylamino)-phenoxy]-benzonitrile; 4-imidazol-1-ylmethyl-2-(3-phenoxy-phenoxy)-benzonitrile; 2-(2-benzoyl-phenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 1-(5-chloro-2-methoxy-phenyl)-3-[3-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-phenyl]-urea; 1-(2,5-

dimethoxy-phenyl)-3-[3-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-phenyl]-urea; 2-(3-benzyloxy-phenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(4-benzyloxy-phenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2-benzyl-phenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3-ethynyl-phenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(4-acetyl-3-methyl-phenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 4-imidazol-1-ylmethyl-2-(1H-indazol-6-yloxy)-benzonitrile; 4-imidazol-1-ylmethyl-2-(5,6,7,8-tetrahydro-naphthalen-1-yloxy)-benzonitrile; 4-imidazol-1-ylmethyl-2-(8-oxo-5,6,7,8-tetrahydro-naphthalen-1-yloxy)-benzonitrile; 4-imidazol-1-ylmethyl-2-(1H-indol-7-yloxy)-benzonitrile; 4-imidazol-1-ylmethyl-2-(3-oxo-indan-4-yloxy)-benzonitrile; 4-imidazol-1-ylmethyl-2-(1H-indol-4-yloxy)-benzonitrile; 2-[3-(2-hydroxy-ethoxy)-phenoxy]-4-imidazol-1-ylmethyl-benzonitrile; 4-imidazol-1-ylmethyl-2-(4-imidazol-1-yl-phenoxy)-benzonitrile; 4-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-biphenyl-4-carbonitrile; N-[3-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-phenyl]-acetamide; 4-imidazol-1-ylmethyl-2-(9-oxo-9H-fluoren-4-yloxy)-benzonitrile; 3-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-Nphenyl-benzamide; 3-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-N-ethyl-N-phenyl-benzamide; 3-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-N-cyclopropylmethyl-N-phenyl-benzamide; 2-(5-chloro-pyridin-3-yloxy)-4-imidazol-1-ylmethyl-benzonitrile; N-[3-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-phenyl]-benzenesulfonamide; 4-imidazol-1-ylmethyl-2-(indan-5-yloxy)-benzonitrile; 3-(9H-carbazol-2-yloxy)-4-imidazol-1-ylmethyl-benzonitrile; 4-imidazol-1-ylmethyl-2-(5,6,7,8-tetrahydro-naphthalen-2-yloxy)-benzonitrile; 4-imidazol-1-ylmethyl-2-(2-methoxy-4-propenyl-phenoxy)-benzonitrile; 4-imidazol-1-ylmethyl-2-[4-(3-oxo-butyl)-phenoxy]-benzonitrile; 2-(3-chlorophenoxy)-5-imidazol-1-ylmethyl-benzonitrile; 2-(4-chlorophenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3,5-dichlorophenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(pyridin-3-yloxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2-chlorophenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(3-chlorophenoxy)-5-(4-phenyl-imidazol-1-ylmethyl)-benzonitrile; 2-(biphen-2-yloxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(phenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2-chloro-4-methoxyphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2-chlorophenylsulfanyl)-4-imidazol-1-ylmethyl-benzonitrile; 4-imidazol-1-ylmethyl-2-(naphthalen-2-ylsulfanyl)-benzonitrile; 2-(2,4-dichlorophenylsulfanyl)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2,4-dichloro-benzenesulfinyl)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2,4-dichloro-benzenesulfonyl)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2-methyl-pyridin-3-yloxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2,4-dimethyl-pyridin-3-yloxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(4-chloro-2-methoxyphenoxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2-chlorophenoxy)-4-(5-methyl-imidazol-1-ylmethyl)-benzonitrile; 2-(2-chlorophenoxy)-4-

(4-methyl-imidazol-1-ylmethyl)-benzonitrile; 2-(3-chloro-5-trifluoromethyl-pyridin-2-yloxy)-4-imidazol-1-ylmethyl-benzonitrile; 2-(2,4-dichlorophenoxy)-4-(2-methyl-imidazol-1-ylmethyl)-benzonitrile; N-[3-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-phenyl]-benzamide; 2-[3-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-phenyl]-N-phenyl-acetamide; 4-imidazol-1-ylmethyl-2-(quinolin-6-yloxy)-benzonitrile; 4-imidazol-1-ylmethyl-2-(2-oxo-1,2-dihydro-quinolin-6-yloxy)-benzonitrile; N-[3-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-phenyl]-2-phenyl-acetamide; 5-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-N-cyclohexyl-nicotinamide; N-(3-chloro-phenyl)-5-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-nicotinamide; 2-(2,3-dimethoxyphenoxy)-4-(2,4-dimethyl-imidazol-1-ylmethyl)-benzonitrile; 4-(2-methyl-imidazol-1-ylmethyl)-2-(naphthalen-2-yloxy)-benzonitrile; 4-(1-imidazol-1-yl-1-methyl-ethyl)-2-(naphthalen-2-yloxy)-benzonitrile; 1-[4-iodo-3-(naphthalen-2-yloxy)-benzyl]-1H-imidazole; acetic acid 3-[3-(2-chloro-phenoxy)-4-cyano-benzyl]-3H-imidazol-4-ylmethyl ester; 2-(2-chloro-phenoxy)-4-(5-hydroxymethyl-imidazol-1-ylmethyl)-benzonitrile; 4-(5-aminomethyl-imidazol-1-ylmethyl)-2-(2-chloro-phenoxy)-benzonitrile; N-{3-[4-cyano-3-(2,3-dimethoxy-phenoxy)-benzyl]-3H-imidazol-4-ylmethyl}-2-cyclohexyl-acetamide; 2-(3-chloro-phenoxy)-4-[(4-chloro-phenyl)-imidazol-1-yl-methyl]-benzonitrile; 2-(3-chloro-phenoxy)-4-[1-(4-chloro-phenyl)-2-hydroxy-1-imidazol-1-yl-ethyl]-benzonitrile; 2-(3-chloro-phenoxy)-4-[(4-chloro-phenyl)-hydroxy-(3H-imidazol-4-yl)-methyl]-benzonitrile; 2-(2,4-dichloro-phenylsulfanyl)-4-[5-(2-morpholin-4-yl-ethyl)-imidazol-1-ylmethyl]-benzonitrile; 2-(2,4-dichloro-phenoxy)-4-[5-(2-morpholin-4-yl-ethyl)-imidazol-1-ylmethyl]-benzonitrile; 4-[hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-2-(naphthalen-2-yloxy)-benzonitrile; 4-[amino-(3-methyl-3H-imidazol-4-yl)-methyl]-2-(naphthalen-2-yloxy)-benzonitrile; 4-[1-hydroxy-1-(3-methyl-3H-imidazol-4-yl)-ethyl]-2-(naphthalen-2-yloxy)-benzonitrile; 4-[1-amino-1-(3-methyl-3H-imidazol-4-yl)-ethyl]-2-(naphthalen-2-yloxy)-benzonitrile hydrochloride; 3-{2-cyano-5-[1-amino-1-(3-methyl-3H-imidazol-4-yl)-ethyl]-phenoxy}-N-ethyl-N-phenyl-benzamide; 3-{2-cyano-5-[1-hydroxy-1-(3-methyl-3H-imidazol-4-yl)-ethyl]-phenoxy}-N-ethyl-N-phenyl-benzamide; 4-[1-hydroxy-1-(3-methyl-3H-imidazol-4-yl)-ethyl]-2-(3-phenylamino-phenoxy)-benzonitrile; 4-[1-hydroxy-1-(3-methyl-3H-imidazol-4-yl)-ethyl]-2-(3-phenoxy-phenoxy)-benzonitrile; 2-(3-benzoyl-phenoxy)-4-[1-hydroxy-1-(3-methyl-3H-imidazol-4-yl)-ethyl]-benzonitrile; 2-(3-tert-butyl-phenoxy)-4-[1-hydroxy-1-(3-methyl-3H-imidazol-4-yl)-ethyl]-benzonitrile; 2-(3-diethylamino-phenoxy)-4-[1-hydroxy-1-(3-methyl-3H-imidazol-4-yl)-ethyl]-benzonitrile; 2-(5-chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethoxy)-4-imidazol-1-ylmethyl-benzonitrile; 4-Imidazol-1-ylmethyl-2-[2-(2-oxo-2H-pyridin-1-yl)-phenoxy]-benzonitrile; 4-Imidazol-1-ylmethyl-2-[3-(2-oxo-2H—pyridin-1-yl)-

phenoxy]-benzonitrile; 4-Imidazol-1-ylmethyl-2-[4-(2-oxo-2H—pyridin-1-yl)-phenoxy]-benzonitrile; 4-imidazol-1-ylmethyl-2-[3-(2-oxo-piperidin-1-yl)-phenoxy]-benzonitrile; 4-imidazol-1-ylmethyl-2-[4-(2-oxo-piperidin-1-yl)-phenoxy]-benzonitrile; 4-imidazol-1-ylmethyl-2-[2-(3-methyl-2-oxo-piperidin-1-yl)-phenoxy]-benzonitrile; 4-imidazol-1-ylmethyl-2-(3-morpholin-4-yl-phenoxy)-benzonitrile; 4-imidazol-1-ylmethyl-2-(3-piperidin-1-ylmethyl-phenoxy)-benzonitrile; 2-[2-(3,3-dimethyl-2-oxo-piperidin-1-yl)-phenoxy]-4-imidazol-1-ylmethyl-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-imidazol-1-ylmethyl-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-(2-methyl-imidazol-1-yl)methyl-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-(5-methyl-imidazol-1-yl)methyl-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-(2,5-dimethyl-imidazol-1-yl)methyl-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-[1,2,4]triazol-4-ylmethyl-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-[1,2,4]triazol-1-ylmethyl-benzonitrile; 4-imidazol-1-ylmethyl-2-[3-(1-methyl-2-oxo-azepan-3-yl)-phenoxy]-benzonitrile; 4-imidazol-1-ylmethyl-2-[3-(1-methyl-2-oxo-azepan-3-yl)-phenoxy]-benzonitrile; 4-imidazol-1-ylmethyl-2-[3-(1-methyl-2-oxo-piperidin-3-yl)-phenoxy]-benzonitrile; 4-imidazol-1-ylmethyl-2-[3-(3-ethyl-1-methyl-2-oxo-piperidin-3-yl)-phenoxy]-benzonitrile; 4-imidazol-1-ylmethyl-2-[3-(2-oxo-azepan-3-yl)-phenoxy]-benzonitrile; 2-[3-(3-hydroxymethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-imidazol-1-ylmethyl-benzonitrile; 2-[3-(3-cyclopropylmethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-imidazol-1-ylmethyl-benzonitrile; 2-[4-bromo-3-(3-cyclopropylmethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-imidazol-1-ylmethyl-benzonitrile; 2-[3-(3-methoxymethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-imidazol-1-ylmethyl-benzonitrile; 2-[3-(3-ethyl-2-oxo-azepan-3-yl)-phenoxy]-4-imidazol-1-ylmethyl-benzonitrile; 2-[3-(3-ethyl-azepan-3-yl)-phenoxy]-4-imidazol-1-ylmethyl-benzonitrile; 2-[3-(1-acetyl-3-ethyl-azepan-3-yl)-phenoxy]-4-imidazol-1-ylmethyl-benzonitrile; 3-[3-(2-cyano-5-imidazol-1-ylmethyl-phenoxy)-phenyl]-3-ethyl-azepane-1-carboxylic acid-tert-butyl ester; 4-[5-(2-amino-ethyl)-2-methyl-imidazol-1-ylmethyl]-2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-[2-methyl-5-(2-morpholin-4-yl-ethyl)-imidazol-1-ylmethyl]-benzonitrile; N-[2-(3-{4-cyano-3-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-benzyl}-2-methyl-3H-imidazol-4-yl)-ethyl]-acetamide; 3-ethyl-3-[3-(3-imidazol-1-ylmethyl-phenoxy)-phenyl]-1-methyl-azepan-2-one; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-(3-methyl-3-H-imidazol-4-ylmethyl)-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-(3H-imidazol-4-ylmethyl)-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-[hydroxy-(3-

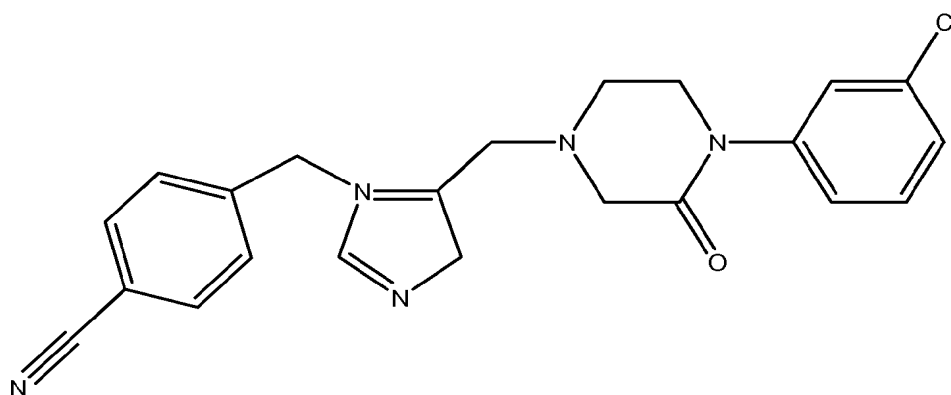
methyl-3-H-imidazol-4-yl)-methyl]-benzonitrile; 4-[amino-(3-methyl-3-H-imidazol-4-yl)-methyl]-2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-benzyl]-4-(3-methyl-3H-imidazole-4-carbonyl)-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-(hydroxy-pyridin-3-yl-methyl)-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-pyridin-3-ylmethyl-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-pyridin-2-ylmethyl-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-[1-hydroxy-1-(3-methyl-3H-imidazol-4-yl)-ethyl]-benzonitrile; 2-[3-(3-ethyl-1-methyl-2-oxo-azepan-3-yl)-phenoxy]-4-[1-amino-1-(3-methyl-3H-imidazol-4-yl)-ethyl]-benzonitrile; 1-[1-(4'-Cyanobenzyl) imidazol-5-ylmethyl]-4-[1-phenyl-1-cyclopentylcarbonyl]piperazine; 1-[1-(4'-Cyanobenzyl) imidazol-5-ylmethyl]-4-[Cyclohexylphenylacetyl]piperazine; 1-[1-(4'-Cyanobenzyl) imidazol-5-ylmethyl]-4-[1-(3-methoxyphenyl)-1-cyclopentylcarbonyl]piperazine; 1-[1-(4'-Cyanobenzyl) imidazol-5-ylmethyl]-4-[1-(3-phenoxyphenyl)-1-cyclopentylcarbonyl]piperazine; 1-[1-(4'-Cyano-3-fluorobenzyl) imidazol-5-ylmethyl]-4-[1-(3-hydroxyphenyl)-1-cyclohexylcarbonyl]piperazine; 1-[1-(4'-Cyanobenzyl) imidazol-5-ylmethyl]piperazine-4-carboxylic acid-(2,6-dimethoxy)benzyl ester; 1-[1-(4'-Cyanobenzyl) imidazol-5-ylmethyl]piperazine-4-(DL-2-hydroxy-2-(o-methoxyphenyl)) acetamide; 1-[1-(4'-Cyanobenzyl) imidazol-5-ylmethyl]-4-[1-(2,6-dimethylbenzyloxycarbonyl]piperazine; 1-[1-(4'-Cyanobenzyl) imidazol-5-ylmethyl]-4-[1-(2-methoxyphenyl)-1-cyclopentylcarbonyl]piperazine; (+/-) 1-[1-(4'-Cyanobenzyl) imidazol-5-ylmethyl]-4-[1-(bicyclo[3.1.0]hex-3-yl)-1-(3-methoxyphenyl)-carbonyl]piperazine; (R/S) 2 [4-((Phenyl)methyloxycarbonyl-1-piperazine)]-2-[1-(4'-cyanobenzyl)-2-methyl-5-imidazol]acetonitrile; 1-[1-(4'-methylbenzyl) imidazol-5-ylmethyl]-4-[1-(2,6-dimethylbenzyloxycarbonyl]piperazine; 1-[1-(4'-Cyanobenzyl) imidazol-5-ylmethyl]piperazine-4-carboxylic acid-(4-nitro)phenyl ester; 1-[1-(4-Cyanobenzyl) imidazol-5-ylmethyl]-4-[3-(4-fluorophenyl)-3-(tricyclo[3.3.1.1^{3,7}]dec-2-yl)-propionyl]piperazine; 2-(1-(4'-cyanobenzyl)imidazol-5-yl-2-[4-(phenylmethyloxy carbonyl)piperazin-1-yl]acetamide; 1-[1-(4'-cyanobenzyl) imidazol-5-ylmethyl]-4-[1-(2-methoxy-5-chlorobenzoyloxycarbonyl]piperazine; 1-[1-(4'-cyanobenzyl) imidazol-5-ylmethyl]-4-[1-(pentafluorobenzoyloxycarbonyl]piperazine; 1-[1-(4'-cyanobenzyl) imidazol-5-ylmethyl]-4-[1-(2-ethoxybenzyloxycarbonyl]piperazine; 1-[1-(4'-cyanobenzyl) imidazol-5-ylmethyl]-4-{1-[(2-methoxypyridin-3-yl)methyloxycarbonyl]}piperazine; 1-[1-(4'-cyanobenzyl) imidazol-5-ylmethyl]-4-[1-(2-trifluoromethoxybenzyloxycarbonyl]piperazine; 1-[1-(4'-cyanobenzyl) imidazol-5-ylmethyl]-4-[1-(2,3-methylenedioxybenzyloxycarbonyl]piperazine; 1-[1-(4'-

Cyanobenzyl) imidazol-5-ylmethyl]piperazine-4-carboxylic acid benzyl ester; 1-[1-(4'-Cyanobenzyl) imidazol-5-ylmethyl]-piperazine-3-carboxylic acid-4-carboxylic acid benzyl ester; 1-[1-(4'-Cyanobenzyl) imidazol-5-ylmethyl]-3-methyl carboxy-piperazine-4-carboxylic acid, or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount.

[00210] In one embodiment, the compound may be one or more of the following: 1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone; (R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone; 4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile and 1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzene, or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount.

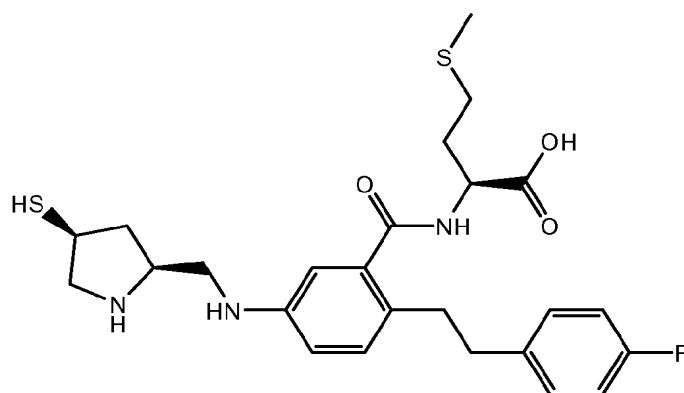
[00211] In another aspect, the invention provides a method of treating a subject with a lysosomal storage disease by administering one or more farnesyl transferase inhibitor compounds described in US Pat No. 5,919,785 and US Pat No. 5,859,012 (the disclosures of which are incorporated herein by reference) or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount.

[00212] In another aspect, the invention provides a method of treating a subject with a lysosomal storage disease by administering a farnesyl transferase inhibitor compound of the formula:



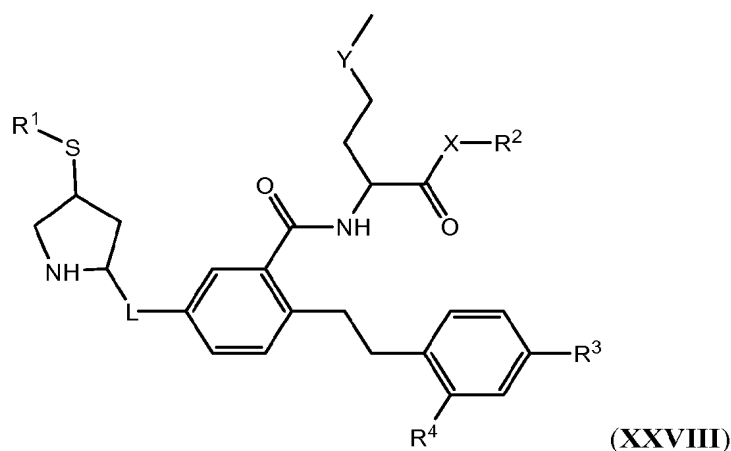
or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount.

[00213] In one embodiment, the invention is a method for treating a subject with a lysosomal storage disease comprising administering to the subject a farnesyl transferase inhibitor of the formula:



or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency.

[00214] In another embodiment, the invention is a method for treating a subject comprising administering to the subject a farnesyl transferase inhibitor of the formula (XXVIII):



wherein

R^1 and R^2 are independently selected from H or a prodrug moiety;

R^3 is hydrogen or halogen;

R^4 is hydrogen or halogen;

X is O or NR^2 ;

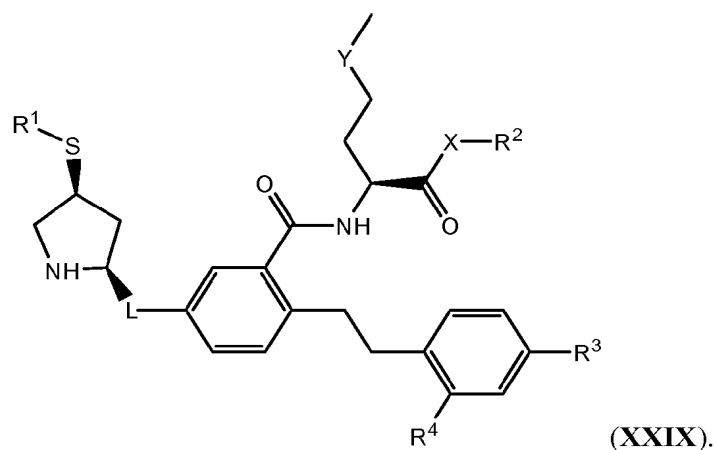
L is $-CH=CH-$ or $-CH_2-Z-$, wherein Z is NH or O;

Y is S, S(O), or S(O)₂;

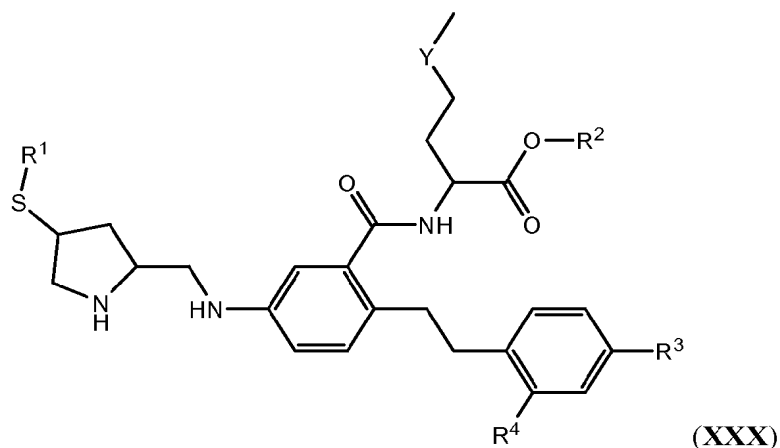
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, at a therapeutically effective dose and frequency. In certain embodiments, a racemate is used in the invention. In other embodiments, an enantiomerically pure compound is used. In other embodiments, an enantiomerically enriched mixture is used (*e.g.*, 70%,

75%, 80%, 90%, 95%, 98%, 99% of one enantiomer). In certain embodiments, the chiral carbon atoms at positions 2 and 4 of the pyrrolidine ring of formula (XXVIII), are of the (*S*)-configuration. In certain embodiments, the chiral carbon atom at position 2 between the carbonyl moiety and the amine in formula (XXVIII) is of the (*S*)-configuration.

[00215] In certain embodiments, the chiral carbon atoms at positions 2 and 4 of the pyrrolidine ring and the chiral carbon atom at position 2 between the carbonyl moiety and the amine of formula (XXVIII) are all of the (*S*)-configuration as shown in the formula (XXIX):

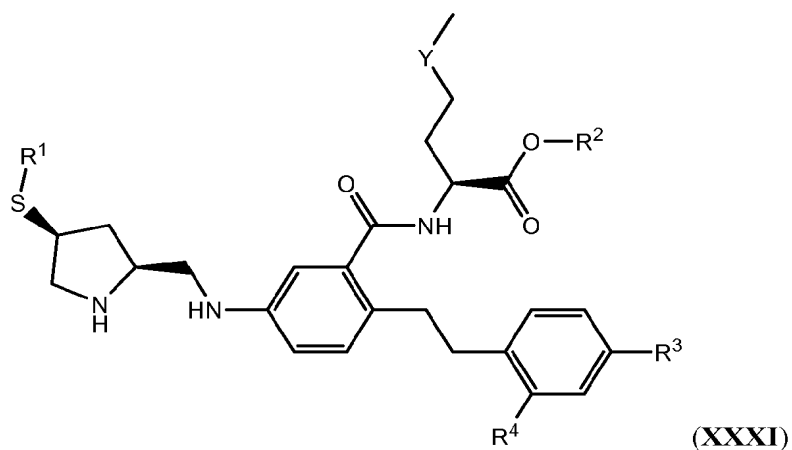


[00216] Compounds useful in the present invention also include compounds of the formula (XXX):



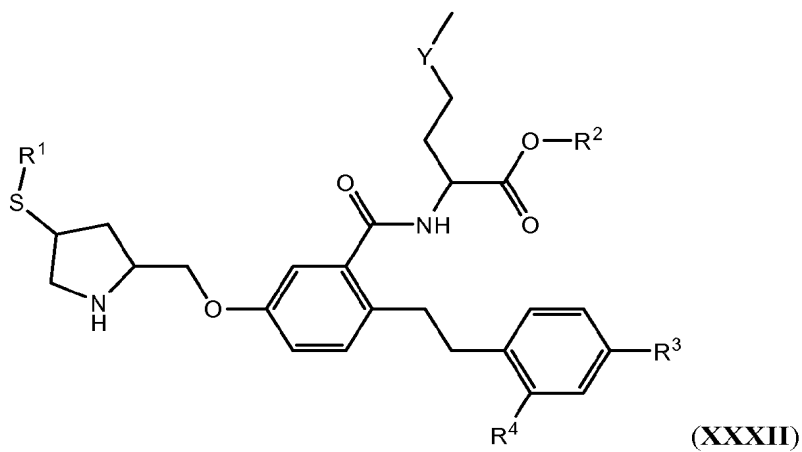
wherein R^1 , R^2 , R^3 , R^4 , and Y are defined as above.

[00217] Compounds useful in the present invention include compounds of the formula (XXX) with the stereochemistry as shown below in formula (XXXI):



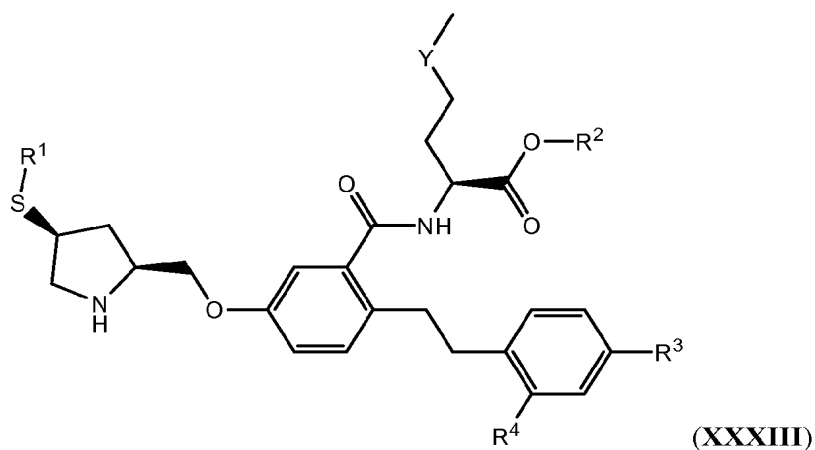
wherein R^1 , R^2 , R^3 , R^4 , and Y are defined as above.

[00218] Compounds useful in the present invention also include compounds of the formula (XXXII):



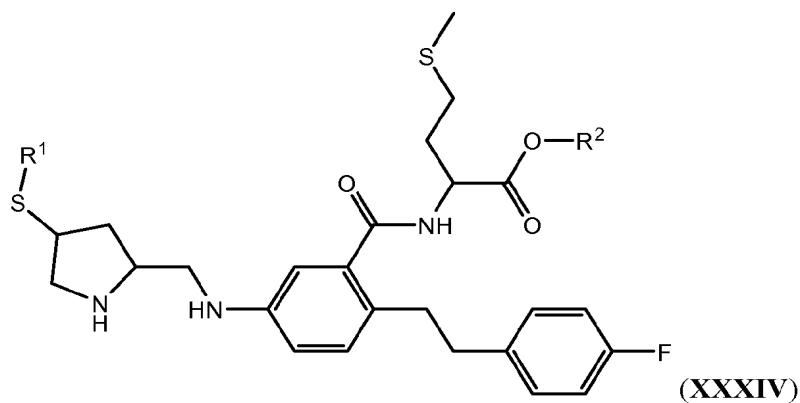
wherein R^1 , R^2 , R^3 , R^4 , and Y are defined as above.

[00219] Compounds useful in the present invention include compounds of the formula (VI) with the stereochemistry as shown below in the formula (XXXIII):



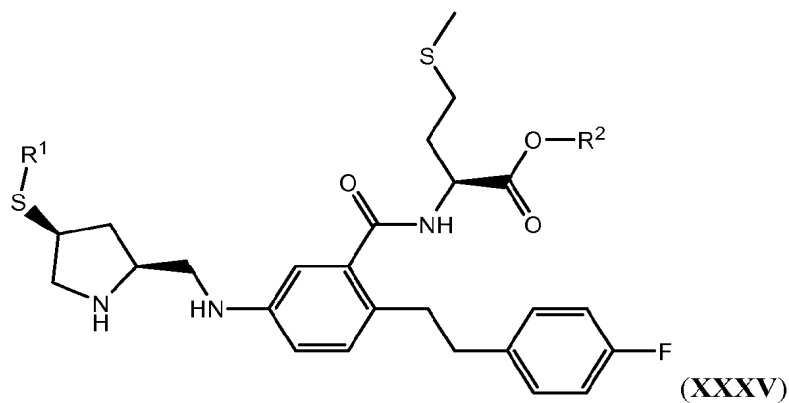
wherein R^1 , R^2 , R^3 , R^4 , and Y are defined as above.

[00220] Compounds useful in the present invention include compounds of the formula (XXXIV):



wherein R^1 and R^2 are defined as above.

[00221] Compounds useful in the present invention include compounds of the formula (XXXIV) with the stereochemistry as shown below in formula (XXXV):



wherein R^1 and R^2 are defined as above.

[00222] In certain classes of the compounds of formulae **XXVIII-XXXV**, R^1 is H or C_1 - C_6 alkyl. In certain compounds useful in the invention, R^1 is H, methyl, ethyl, *iso*-propyl, or *n*-propyl. In certain particular compounds, R^1 is hydrogen.

[00223] In certain classes of the compounds of formulae **XXVIII-XXXV**, R^1 is acyl. In certain embodiments, R^1 is $-C(O)R^5$, wherein R^5 is substituted or unsubstituted, branched or unbranched, cyclic or acyclic aliphatic; substituted or unsubstituted, branched or unbranched, cyclic or acyclic heteroaliphatic; substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. In certain compounds, R^5 is an optionally substituted aryl, heteroaryl, carbocyclic, or heterocyclic moiety. In certain particular embodiments, R^5 is an optionally substituted phenyl, pyridyl, furyl, isoxazole, tetrahydropyridyl, or tetrahydrofuryl ring. In certain particular embodiments, R^5 is phenyl, pyridyl, or N-methylpiperidine. In other embodiments, R^5 is an optionally substituted C_1 - C_6 alkyl group. In certain embodiments, R^5 is methyl. In other embodiments, R^5 is hydroxy, alkoxy, or cyano.

[00224] In certain classes of compounds of formula **XXVIII-XXXV**, R^2 is H or C_1 - C_6 alkyl. In certain compounds useful in the invention, R^2 is H, methyl, ethyl, *iso*-propyl, or *n*-propyl. In certain particular compounds, R^2 is hydrogen. In certain particular compounds, R^2 is an optionally substituted heterocyclic group such as N-methyl-tetrahydropyridyl.

[00225] In certain classes of compounds of formula **XXVIII-XXXV**, wherein X is O, $-C(O)OR^2$ is an *in vivo* cleavable ester group of a pharmaceutically acceptable ester which is cleaved *in vivo* to produce the parent acid. In certain embodiments, R^2 is substituted or unsubstituted, branched or unbranched, cyclic or acyclic aliphatic; substituted or unsubstituted, branched or unbranched, cyclic or acyclic heteroaliphatic; substituted or unsubstituted aryl; or substituted or unsubstituted heteroaryl. Suitably R^2 together with the carboxy group to which it is attached (*i.e.*, $-C(O)OR^2$) forms a pharmaceutically-acceptable esters such as C_{1-6} alkyl esters or C_{1-6} cycloalkyl esters, for example methyl, ethyl, propyl, *iso*-propyl, *n*-butyl or cyclopentyl; C_{1-6} alkoxymethyl esters, for example methoxymethyl; C_{1-6} alkanoyloxymethyl esters, for example pivaloyloxymethyl; phthalidyl esters; C_{3-8} cycloalkoxycarbonyloxy C_{1-6} alkyl esters, for example 1-cyclohexylcarbonyloxyethyl; 1,3-dioxolan-2-ylmethyl esters, for example 5-methyl-1,3-dioxolan-2-ylmethyl; C_{1-6} alkoxycarbonyloxyethyl esters, for example 1-methoxycarbonyloxyethyl; aminocarbonylmethyl esters and mono- or di- N-(C_{1-6} alkyl) versions thereof, for example N,N-dimethylaminocarbonylmethyl esters and N-ethylaminocarbonylmethyl esters, and pharmaceutically acceptable esters of optionally substituted heterocyclic groups.

[00226] In other classes of compounds of formula **XXVIII-XXXV**, when X is NR^2 , $-\text{C}(\text{O})\text{N}(\text{R}^2)_2$ is an *in vivo* cleavable amide group. Suitably R^2 together with the carboxy group to which it is attached (*i.e.*, $-\text{C}(\text{O})\text{N}(\text{R}^2)_2$) forms a pharmaceutically-acceptable amide, preferably an N- C_{1-6} alkylamide and an N,N-di- $(\text{C}_{1-6}$ alkyl)amide, such as N-methyl, N-ethyl, N-propyl, N,N-dimethyl, N-ethyl-N-methyl or N,N-diethylamide.

[00227] In other classes of the compounds of formula **XXVIII-XXXV**, R^3 is hydrogen. In certain other classes, R^3 is a halogen. In yet other classes, R^3 is fluorine. In other classes, R^3 is chlorine.

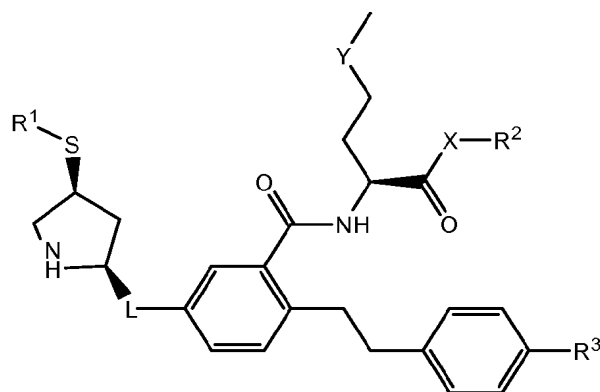
[00228] In other classes of the compounds of formula **XXVIII-XXXV**, R^4 is hydrogen. In certain other classes, R^4 is a halogen. In yet other classes, R^4 is fluorine. In other classes, R^4 is chlorine.

[00229] In certain classes of compounds of formula **XXVIII-XXIX**, X is O. In other classes, X is NR^2 . In other particular classes, X is NH.

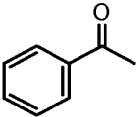
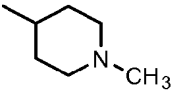
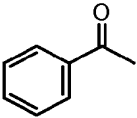
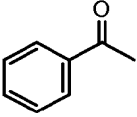
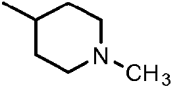
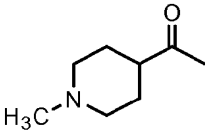
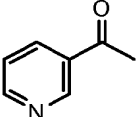
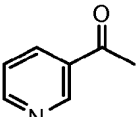
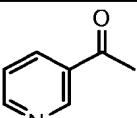
[00230] In certain classes of the compounds of formula **XXVIII-XXIX**, L is $-\text{CH}=\text{CH}-$. In other classes, L is $-\text{CH}_2-\text{O}-$. In other classes, L is $-\text{CH}_2-\text{NH}-$.

[00231] In yet other classes of the compounds of formula **XXVIII-XXXV**, Y is S. In other classes, Y is $\text{S}(\text{O})$. In still other classes, Y is $\text{S}(\text{O})_2$.

[00232] Particular examples of compounds useful in the present invention are shown in the Table below:



<u>Compd. No.</u>	<u>R¹</u>	<u>R²</u>	<u>R³</u>	<u>L</u>	<u>Y</u>
1	H	H	F	$-\text{CH}_2\text{NH}-$	S
2	H	$-\text{CH}(\text{CH}_3)_2$	F	$-\text{CH}_2\text{NH}-$	S

<u>Compd. No.</u>	<u>R¹</u>	<u>R²</u>	<u>R³</u>	<u>L</u>	<u>Y</u>
3			F	-CH ₂ O-	S
4		-CH(CH ₃) ₂	F	-CH ₂ NH-	S
5			F	-CH ₂ NH-	S
6		-CH(CH ₃) ₂	F	-CH ₂ NH-	S
7		-CH(CH ₃) ₂	F	-CH ₂ O-	SO ₂
8		-CH(CH ₃) ₂	F	-CH ₂ CH-	S
9		-CH(CH ₃) ₂	F	-CH=CH-	S

[00233] As used herein, the term “subject with a lysosomal storage disease” refers to a subject that is diagnosed with, affected by, or at risk of developing a lysosomal storage disease. Exemplary lysosomal storage disorders include Farber disease, Niemann-Pick disease, Gaucher disease, Fabry disease, Krabbe disease, and Pompe disease.

[00234] The invention provides methods for treating lysosomal storage diseases using inhibitors of farnesyl transferase. It has been now discovered that UCH-L1 is farnesylated *in vivo*. UCH-L1 is associated with the membrane and this membrane association is mediated by farnesylation. The invention relates to the prevention or inhibition of UCH-L1

farnesylation which would result in UCH-L1 membrane disassociation and acceleration of the degradation of substrates or proteins which accumulate in lysosomal storage diseases. In the case of a deficiency of a lysosomal enzyme, substrate accumulation is usually pathogenic, and an increased degradation of the substrate ameliorates the toxicity associated with a pathogenic accumulation of the substrate. In the case of a deficiency of a lysosomal non-enzyme protein which is involved in trafficking, processing, activation, or stabilisation of a lysosomal enzyme, substrate accumulation usually occurs and an increased degradation of the substrate ameliorates the toxicity associated with a pathogenic accumulation of the substrate. In the case of a deficiency of a lysosomal protein unrelated to a particular enzyme activity *per se* but involved in lysosomal function, general lysosomal dysfunction and protein or organelle accumulation can occur causing toxicity, and an increased degradation of accumulated proteins or organelles ameliorates the toxicity.

[00235] The modification of a protein by a farnesyl group can have an important effect on function for a number of proteins. Farnesylated proteins typically undergo further C-terminal modification events that include a proteolytic removal of three C-terminal amino acids and carboxymethylation of C-terminal cystines. These C-terminal modifications facilitate protein-membrane association as well as protein-protein interactions. Farnesylation is catalyzed by a protein farnesyltransferase (FTase), a heterodimeric enzyme that recognizes the CAAX motif present at the C-terminus of the substrate protein. FTase transfers a farnesyl group from farnesyl pyrophosphate and forms a thioether linkage between the farnesyl and the cystine residues in the CAAX motif. A number of inhibitors of FTase have been developed and are known in the art. However, the invention provides novel methods for using certain farnesyl transferase inhibitors to treat subjects having symptoms associated with substrate, protein, or organelle accumulation found in lysosomal storage diseases.

[00236] Methods of the invention can be used in combination with one or more other medications, including medications that are currently used to treat lysosomal storage diseases or symptoms arising as side-effects of the disease or of the aforementioned medications.

[00237] According to the invention, the term “treatment” includes prophylaxis and therapy, and includes managing a subject’s symptoms and halting the progression of the disease. Treatment includes preventing, slowing, stopping, or reversing (*e.g.*, curing) the development of a lysosomal storage disease, and/or the onset of certain symptoms associated with a lysosomal storage disease in a subject with, or at risk of developing a lysosomal storage disease or a related disorder. For the treatment of a lysosomal storage disease, the therapy typically includes preventing, slowing, stopping, or reversing (*e.g.*, curing) the

accumulation of the substrate resulting from the enzyme deficiency associated with the lysosomal storage disease. Therapy also includes decreasing the amount of accumulated substrate in a subject with a lysosomal storage disease. Therapy may also include preventing, slowing, stopping, or reversing the signs and symptoms associated with the lysosomal storage disease.

[00238] The phrase “therapeutically-effective amount” as used herein means that amount of a compound, material, or composition comprising a compound of the present invention which is effective for producing some desired therapeutic effect in a subject at a reasonable benefit/risk ratio applicable to any medical treatment. Accordingly, a therapeutically effective amount prevents, minimizes, or reverses disease progression associated with a lysosomal storage disease. Disease progression can be monitored by clinical observations, laboratory, and imaging investigations apparent to a person skilled in the art. A therapeutically effective amount can be an amount that is effective in a single dose or an amount that is effective as part of a multi-dose therapy, for example an amount that is administered in two or more doses or an amount that is administered chronically.

[00239] The “pharmaceutically acceptable acid or base addition salts” mentioned herein are meant to comprise the therapeutically active non-toxic acid and non-toxic base addition salt forms that the compounds are able to form. The compounds that have basic properties can be converted into their pharmaceutically acceptable acid addition salts by treating the base form with an appropriate acid. Appropriate acids include, for example, inorganic acids such as hydrohalic acids, *e.g.*, hydrochloric or hydrobromic acid; sulfuric; nitric; phosphoric and the like acids; or organic acids such as, for example, acetic, propanoic, hydroxyacetic, lactic, pyruvic, oxalic, malonic, succinic (*i.e.*, butanedioic acid), maleic, fumaric, malic, tartaric, citric, methanesulfonic, ethanesulfonic, benzenesulfonic, *p*-toluenesulfonic, cyclamic, salicylic, *p*-aminosalicylic, pamoic and the like acids. In certain embodiments, the salt is a tartrate salt. The tartrate salt may be either L-tartric acid or D-tartric acid. Both tartric acids are available from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin). The salts may be anhydrous or hydrous forms.

[00240] The compounds that have acidic properties can be converted into their pharmaceutically acceptable base addition salts by treating the acid form with a suitable organic or inorganic base. Appropriate base salt forms include, for example, the ammonium salts, the alkali and earth alkaline metal salts, *e.g.*, the lithium, sodium, potassium, magnesium, calcium salts and the like, salts with organic bases, *e.g.*, the benzathine, N-

methyl-D-glucamine, hydrabamine salts, and salts with amino acids such as, for example, arginine, lysine, and the like.

[00241] The terms acid or base addition salt also comprise the hydrates and the solvent addition forms which the compounds are able to form. Examples of such forms are, *e.g.*, hydrates, alcoholates, and the like.

[00242] The term stereochemically isomeric forms of compounds, as used herein, include all possible compounds made up of the same atoms bonded by the same sequence of bonds but having different three-dimensional structures which are not interchangeable, which the compounds may possess. Unless otherwise mentioned or indicated, the chemical designation of a compound encompasses the mixture of all possible stereochemically isomeric forms that the compound can take. The mixture can contain all diastereomers and/or enantiomers of the basic molecular structure of the compound. All stereochemically isomeric forms of the compounds both in pure form or in admixture with each other are intended to be embraced within the scope of the present invention.

[00243] Some of the compounds may also exist in their tautomeric forms. Such forms although not explicitly indicated in the above formula are intended to be included within the scope of the present invention.

[00244] The methods and structures described herein relating to compounds and compositions of the invention also apply to the pharmaceutically acceptable acid or base addition salts and all stereoisomeric forms of these compounds and compositions.

[00245] In the compounds and compositions of the invention, the term “alkyl” refers to the radical of saturated aliphatic groups, including straight-chain alkyl groups, branched-chain alkyl groups, cycloalkyl (alicyclic) groups, alkyl substituted cycloalkyl groups, and cycloalkyl substituted alkyl groups. In preferred embodiments, a straight chain or branched chain alkyl has 12 or fewer carbon atoms in its backbone (*e.g.*, C₁-C₁₂ for straight chain, C₃-C₁₂ for branched chain), and more preferably 6 or fewer, and even more preferably 4 or fewer. Likewise, preferred cycloalkyls have from 3-10 carbon atoms in their ring structure, and more preferably have 5, 6, or 7 carbons in the ring structure.

[00246] Unless the number of carbons is otherwise specified, “lower alkyl” as used herein means an alkyl group, as defined above, but having from one to ten carbons, more preferably from one to six carbon atoms in its backbone structure, and even more preferably from one to four carbon atoms in its backbone structure. Likewise, “lower alkenyl” and “lower alkynyl” have similar chain lengths. Preferred alkyl groups are lower alkyls. In preferred embodiments, a substituent designated herein as alkyl is a lower alkyl.

[00247] As used herein, the term “halogen” designates -F, -Cl, -Br or -I; the term “sulfhydryl” means -SH; and the term “hydroxyl” means -OH.

[00248] The term “methyl” refers to the monovalent radical -CH₃, and the term “methoxyl” refers to the monovalent radical -CH₂OH.

[00249] The term “aralkyl” or “arylalkyl”, as used herein, refers to an alkyl group substituted with an aryl group (*e.g.*, an aromatic or heteroaromatic group).

[00250] The terms “alkenyl” and “alkynyl” refer to unsaturated aliphatic groups analogous in length and possible substitution to the alkyls described above, but that contain at least one double or triple bond respectively.

[00251] The term “aryl” as used herein includes 5-, 6- and 7-membered single-ring aromatic groups that may include from zero to four heteroatoms, for example, benzene, pyrrole, furan, thiophene, imidazole, oxazole, thiazole, triazole, pyrazole, pyridine, pyrazine, pyridazine and pyrimidine, and the like. Those aryl groups having heteroatoms in the ring structure may also be referred to as “aryl heterocycles” or “heteroaromatics.” The aromatic ring can be substituted at one or more ring positions with such substituents as described above, for example, halogen, azide, alkyl, aralkyl, alkenyl, alkynyl, cycloalkyl, hydroxyl, alkoxy, amino, nitro, sulfhydryl, imino, amido, phosphonate, phosphinate, carbonyl, carboxyl, silyl, ether, alkylthio, sulfonyl, sulfonamido, ketone, aldehyde, ester, heterocyclyl, aromatic or heteroaromatic moieties, -CF₃, -CN, or the like. The term “aryl” also includes polycyclic ring systems having two or more cyclic rings in which two or more carbons are common to two adjoining rings (the rings are “fused rings”) wherein at least one of the rings is aromatic, *e.g.*, the other cyclic rings can be cycloalkyls, cycloalkenyls, cycloalkynyls, aryls and/or heterocyclyls.

[00252] The terms “ortho”, “meta”, and “para” apply to 1,2-, 1,3- and 1,4-disubstituted benzenes, respectively. For example, the names 1,2-dimethylbenzene and ortho-dimethylbenzene are synonymous.

[00253] The terms “heterocyclyl” or “heterocyclic group” or “heteroaryl” refer to 3- to 10-membered ring structures, more preferably 3- to 7-membered rings, whose ring structures include one to four heteroatoms. Heterocycles can also be polycycles. Heterocyclyl groups include, for example, thiophene, benzothiophene, thianthrene, furan, pyran, isobenzofuran, chromene, xanthene, phenoxathiin, pyrrole, imidazole, pyrazole, isothiazole, isoxazole, pyridine, pyrazine, pyrimidine, pyridazine, indolizine, isoindole, indole, indazole, purine, quinolizine, isoquinoline, quinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, carbazole, carboline, phenanthridine, acridine, pyrimidine,

phenanthroline, phenazine, phenarsazine, phenothiazine, furazan, phenoxazine, pyrrolidine, oxolane, thiolane, oxazole, piperidine, piperazine, morpholine, lactones, lactams such as azetidinones and pyrrolidinones, sultams, sultones, and the like. The heterocyclic ring can be substituted at one or more positions with such substituents as described above, as for example, halogen, alkyl, aralkyl, alkenyl, alkynyl, cycloalkyl, hydroxyl, amino, nitro, sulfhydryl, imino, amido, phosphonate, phosphinate, carbonyl, carboxyl, silyl, ether, alkylthio, sulfonyl, ketone, aldehyde, ester, a heterocyclyl, an aromatic or heteroaromatic moiety, -CF₃, -CN, or the like.

[00254] As used herein, the definition of each expression, *e.g.*, alkyl, m, n, *etc.*, when it occurs more than once in any structure, is intended to be independent of its definition elsewhere in the same structure.

[00255] It will be understood that "substitution" or "substituted with" includes the implicit proviso that such substitution is in accordance with permitted valence of the substituted atom and the substituent, and that the substitution results in a stable compound, *e.g.*, which does not spontaneously undergo transformation such as by rearrangement, cyclization, elimination, *etc.*

[00256] As used herein, the term "substituted" is contemplated to include all permissible substituents of organic compounds. In a broad aspect, the permissible substituents include acyclic and cyclic, branched and unbranched, carbocyclic and heterocyclic, aromatic and nonaromatic substituents of organic compounds. Illustrative substituents include, for example, those described herein above. The permissible substituents can be one or more and the same or different for appropriate organic compounds. For purposes of this invention, the heteroatoms such as nitrogen may have hydrogen substituents and/or any permissible substituents of organic compounds described herein which satisfy the valences of the heteroatoms. This invention is not intended to be limited in any manner by the permissible substituents of organic compounds.

[00257] Certain compounds of the present invention may exist in particular geometric or stereoisomeric forms. The present invention contemplates all such compounds, including *cis*- and *trans*-isomers, R- and S-enantiomers, diastereomers, (D)-isomers, (L)-isomers, the racemic mixtures thereof, and other mixtures thereof, as falling within the scope of the invention. Additional asymmetric carbon atoms may be present in a substituent such as an alkyl group. All such isomers, as well as mixtures thereof, are intended to be included in this invention. In certain embodiments, the present invention relates to a compound represented by any of the structures outlined herein, wherein the compound is a single stereoisomer.

[00258] If, for instance, a particular enantiomer of a compound of the present invention is desired, it may be prepared by asymmetric synthesis, or by derivation with a chiral auxiliary, where the resulting diastereomeric mixture is separated and the auxiliary group cleaved to provide the pure desired enantiomers. Alternatively, where the molecule contains a basic functional group, such as amino, or an acidic functional group, such as carboxyl, diastereomeric salts are formed with an appropriate optically-active acid or base, followed by resolution of the diastereomers thus formed by fractional crystallization or chromatographic means well known in the art, and subsequent recovery of the pure enantiomers.

[00259] Contemplated equivalents of the compounds described above include compounds which otherwise correspond thereto, and which have the same general properties thereof (*e.g.*, functioning as farnesyl transferase inhibitor compounds for treating lysosomal storage diseases), wherein one or more simple variations of substituents are made which do not adversely affect the efficacy of the compound. In general, the compounds of the present invention may be prepared by the methods illustrated in the general reaction schemes as, for example, described below, or by modifications thereof, using readily available starting materials, reagents and conventional synthesis procedures. In these reactions, it is also possible to make use of variants, which are in themselves known, but are not mentioned here.

[00260] For purposes of this invention, the chemical elements are identified in accordance with the Periodic Table of the Elements, CAS version, *Handbook of Chemistry and Physics*, 67th Ed., 1986-87, inside cover.

[00261] In another aspect, the present invention provides "pharmaceutically acceptable" compositions, which comprise a therapeutically effective amount of one or more of the compounds described herein, formulated together with one or more pharmaceutically acceptable carriers (additives) and/or diluents. As described in detail, the pharmaceutical compositions of the present invention may be specially formulated for administration in solid or liquid form, including those adapted for the following: oral administration, for example, drenches (aqueous or non-aqueous solutions or suspensions), tablets, *e.g.*, those targeted for buccal, sublingual, and systemic absorption, boluses, powders, granules, pastes for application to the tongue; parenteral administration, for example, by subcutaneous, intramuscular, intravenous, or epidural injection as, for example, a sterile solution or suspension, or sustained-release formulation; topical application, for example, as a cream, ointment, or a controlled-release patch or spray applied to the skin, lungs, or oral cavity; intravaginally or intrarectally, for example, as a pessary, cream or foam; sublingually; ocularly; transdermally; or nasally, pulmonary, and to other mucosal surfaces.

[00262] The phrase “pharmaceutically acceptable” is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

[00263] The phrase “pharmaceutically-acceptable carrier” as used herein means a pharmaceutically-acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, or solvent encapsulating material, involved in carrying or transporting the subject compound from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be “acceptable” in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient. Some examples of materials which can serve as pharmaceutically-acceptable carriers include: sugars, such as lactose, glucose and sucrose; starches, such as corn starch and potato starch; cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients, such as cocoa butter and suppository waxes; oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene glycol; polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; esters, such as ethyl oleate and ethyl laurate; agar; buffering agents, such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline; Ringer’s solution; ethyl alcohol; pH buffered solutions; polyesters, polycarbonates and/or polyanhydrides; and other non-toxic compatible substances employed in pharmaceutical formulations.

[00264] As set out herein, certain embodiments of the present compounds may contain a basic functional group, such as amino or alkylamino, and are, thus, capable of forming pharmaceutically-acceptable salts with pharmaceutically-acceptable acids. The term “pharmaceutically-acceptable salts” in this respect refers to the relatively non-toxic, inorganic and organic acid addition salts of compounds of the present invention. These salts can be prepared *in situ* in the administration vehicle or the dosage form manufacturing process, or by separately reacting a purified compound of the invention in its free base form with a suitable organic or inorganic acid, and isolating the salt thus formed during subsequent purification. Representative salts include the hydrobromide, hydrochloride, sulfate, bisulfate, phosphate, nitrate, acetate, valerate, oleate, palmitate, stearate, laurate, benzoate, lactate, phosphate, tosylate, citrate, maleate, fumarate, succinate, tartrate, naphthylate, mesylate, glucoheptonate,

lactobionate, and laurylsulphonate salts and the like. (See, for example, Berge *et al.* (1977) "Pharmaceutical Salts", *J. Pharm. Sci.* 66:1-19; incorporated herein by reference)

[00265] The pharmaceutically acceptable salts of the subject compounds include the conventional nontoxic salts or quaternary ammonium salts of the compounds, *e.g.*, from non-toxic organic or inorganic acids. For example, such conventional nontoxic salts include those derived from inorganic acids such as hydrochloride, hydrobromic, sulfuric, sulfamic, phosphoric, nitric, and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, palmitic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isothionic, and the like.

[00266] In other cases, the compounds of the present invention may contain one or more acidic functional groups and, thus, are capable of forming pharmaceutically-acceptable salts with pharmaceutically-acceptable bases. The term "pharmaceutically-acceptable salts" in these instances refers to the relatively non-toxic, inorganic and organic base addition salts of compounds of the present invention. These salts can likewise be prepared *in situ* in the administration vehicle or the dosage form manufacturing process, or by separately reacting the purified compound in its free acid form with a suitable base, such as the hydroxide, carbonate or bicarbonate of a pharmaceutically-acceptable metal cation, with ammonia, or with a pharmaceutically-acceptable organic primary, secondary or tertiary amine. Representative alkali or alkaline earth salts include the lithium, sodium, potassium, calcium, magnesium, and aluminum salts and the like. Representative organic amines useful for the formation of base addition salts include ethylamine, diethylamine, ethylenediamine, ethanolamine, diethanolamine, piperazine and the like. (See, for example, Berge *et al.*, *supra*).

[00267] Wetting agents, emulsifiers and lubricants, such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, release agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants can also be present in the compositions.

[00268] Examples of pharmaceutically-acceptable antioxidants include: water soluble antioxidants, such as ascorbic acid, cysteine hydrochloride, sodium bisulfate, sodium metabisulfite, sodium sulfite and the like; oil-soluble antioxidants, such as ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, propyl gallate, alpha-tocopherol, and the like; and metal chelating agents, such as citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid, and the like.

[00269] Formulations of the present invention include those suitable for oral, nasal, topical (including buccal and sublingual), rectal, vaginal and/or parenteral administration. The formulations may conveniently be presented in unit dosage form and may be prepared by any methods well known in the art of pharmacy. The amount of active ingredient which can be combined with a carrier material to produce a single dosage form will vary depending upon the host being treated, and the particular mode of administration. The amount of active ingredient that can be combined with a carrier material to produce a single dosage form will generally be that amount of the compound which produces a therapeutic effect. Generally, this amount will range from about 1% to about 99% of active ingredient, preferably from about 5% to about 70%, most preferably from about 10% to about 30%.

[00270] In certain embodiments, a formulation of the present invention comprises an excipient selected from the group consisting of cyclodextrins, liposomes, micelle forming agents, *e.g.*, bile acids, and polymeric carriers, *e.g.*, polyesters and polyanhydrides; and a compound of the present invention. In certain embodiments, an aforementioned formulation renders orally bioavailable a compound of the present invention.

[00271] Methods of preparing these formulations or compositions include the step of bringing into association a compound of the present invention with the carrier and, optionally, one or more accessory ingredients. In general, the formulations are prepared by uniformly and intimately bringing into association a compound of the present invention with liquid carriers, or finely divided solid carriers, or both, and then, if necessary, shaping the product.

[00272] Formulations of the invention suitable for oral administration may be in the form of capsules, cachets, pills, tablets, lozenges (using a flavored basis, usually sucrose and acacia or tragacanth), powders, granules, or as a solution or a suspension in an aqueous or non-aqueous liquid, or as an oil-in-water or water-in-oil liquid emulsion, or as an elixir or syrup, or as pastilles (using an inert base, such as gelatin and glycerin, or sucrose and acacia) and/or as mouth washes and the like, each containing a predetermined amount of a compound of the present invention as an active ingredient. A compound of the present invention may also be administered as a bolus, electuary or paste.

[00273] In solid dosage forms of the invention for oral administration (capsules, tablets, pills, dragees, powders, granules and the like), the active ingredient is mixed with one or more pharmaceutically-acceptable carriers, such as sodium citrate or dicalcium phosphate, and/or any of the following: fillers or extenders, such as starches, lactose, sucrose, glucose, mannitol, and/or silicic acid; binders, such as, for example, carboxymethylcellulose,

alginates, gelatin, polyvinyl pyrrolidone, sucrose and/or acacia; humectants, such as glycerol; disintegrating agents, such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate; solution retarding agents, such as paraffin; absorption accelerators, such as quaternary ammonium compounds; wetting agents, such as, for example, cetyl alcohol, glycerol monostearate, and non-ionic surfactants; absorbents, such as kaolin and bentonite clay; lubricants, such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof; and coloring agents. In the case of capsules, tablets and pills, the pharmaceutical compositions may also comprise buffering agents. Solid compositions of a similar type may also be employed as fillers in soft and hard-shelled gelatin capsules using such excipients as lactose or milk sugars, as well as high molecular weight polyethylene glycols and the like.

[00274] A tablet may be made by compression or molding, optionally with one or more accessory ingredients. Compressed tablets may be prepared using binder (for example, gelatin or hydroxypropylmethyl cellulose), lubricant, inert diluent, preservative, disintegrant (for example, sodium starch glycolate or cross-linked sodium carboxymethyl cellulose), surface-active or dispersing agent. Molded tablets may be made in a suitable machine in which a mixture of the powdered compound is moistened with an inert liquid diluent.

[00275] The tablets, and other solid dosage forms of the pharmaceutical compositions of the present invention, such as dragees, capsules, pills and granules, may optionally be scored or prepared with coatings and shells, such as enteric coatings and other coatings well known in the pharmaceutical-formulating art. They may also be formulated so as to provide slow or controlled release of the active ingredient therein using, for example, hydroxypropylmethyl cellulose in varying proportions to provide the desired release profile, other polymer matrices, liposomes and/or microspheres. They may be formulated for rapid release, e.g., freeze-dried. They may be sterilized by, for example, filtration through a bacteria-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions that can be dissolved in sterile water, or some other sterile injectable medium immediately before use. These compositions may also optionally contain opacifying agents and may be of a composition that they release the active ingredient(s) only, or preferentially, in a certain portion of the gastrointestinal tract, optionally, in a delayed manner. Examples of embedding compositions that can be used include polymeric substances and waxes. The active ingredient can also be in micro-encapsulated form, if appropriate, with one or more of the above-described excipients.

[00276] Liquid dosage forms for oral administration of the compounds of the invention include pharmaceutically acceptable emulsions, microemulsions, solutions, suspensions, syrups and elixirs. In addition to the active ingredient, the liquid dosage forms may contain inert diluents commonly used in the art, such as, for example, water or other solvents, solubilizing agents and emulsifiers, such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor and sesame oils), glycerol, tetrahydrofuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan, and mixtures thereof.

[00277] Besides inert diluents, the oral compositions can also include adjuvants such as wetting agents, emulsifying and suspending agents, sweetening, flavoring, coloring, perfuming and preservative agents.

[00278] Suspensions, in addition to the active compounds, may contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth, and mixtures thereof.

[00279] Formulations of the pharmaceutical compositions of the invention for rectal or vaginal administration may be presented as a suppository, which may be prepared by mixing one or more compounds of the invention with one or more suitable nonirritating excipients or carriers comprising, for example, cocoa butter, polyethylene glycol, a suppository wax or a salicylate, and which is solid at room temperature, but liquid at body temperature and, therefore, will melt in the rectum or vaginal cavity and release the active compound.

[00280] Formulations of the present invention which are suitable for vaginal administration also include pessaries, tampons, creams, gels, pastes, foams or spray formulations containing such carriers as are known in the art to be appropriate.

[00281] Dosage forms for the topical or transdermal administration of a compound of this invention include powders, sprays, ointments, pastes, creams, lotions, gels, solutions, patches and inhalants. The active compound may be mixed under sterile conditions with a pharmaceutically-acceptable carrier, and with any preservatives, buffers, or propellants which may be required.

[00282] The ointments, pastes, creams and gels may contain, in addition to an active compound of this invention, excipients, such as animal and vegetable fats, oils, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones, bentonites, silicic acid, talc and zinc oxide, or mixtures thereof.

[00283] Powders and sprays can contain, in addition to a compound of this invention, excipients such as lactose, talc, silicic acid, aluminum hydroxide, calcium silicates and polyamide powder, or mixtures of these substances. Sprays can additionally contain customary propellants, such as chlorofluorohydrocarbons and volatile unsubstituted hydrocarbons, such as butane and propane.

[00284] Transdermal patches have the added advantage of providing controlled delivery of a compound of the present invention to the body. Dissolving or dispersing the compound in the proper medium can make such dosage forms. Absorption enhancers can also be used to increase the flux of the compound across the skin. Either providing a rate controlling membrane or dispersing the compound in a polymer matrix or gel can control the rate of such flux.

[00285] Ophthalmic formulations, eye ointments, powders, solutions and the like, are also contemplated as being within the scope of this invention.

[00286] Pharmaceutical compositions of this invention suitable for parenteral administration comprise one or more compounds of the invention in combination with one or more pharmaceutically-acceptable sterile isotonic aqueous or nonaqueous solutions, dispersions, suspensions or emulsions, or sterile powders which may be reconstituted into sterile injectable solutions or dispersions just prior to use, which may contain sugars, alcohols, antioxidants, buffers, bacteriostats, solutes which render the formulation isotonic with the blood of the intended recipient or suspending or thickening agents.

[00287] Examples of suitable aqueous and nonaqueous carriers, which may be employed in the pharmaceutical compositions of the invention include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol, and the like), and suitable mixtures thereof, vegetable oils, such as olive oil, and injectable organic esters, such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of coating materials, such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants.

[00288] These compositions may also contain adjuvants such as preservatives, wetting agents, emulsifying agents and dispersing agents. Prevention of the action of microorganisms upon the subject compounds may be ensured by the inclusion of various antibacterial and antifungal agents, for example, paraben, chlorobutanol, phenol sorbic acid, and the like. It may also be desirable to include isotonic agents, such as sugars, sodium chloride, and the like into the compositions. In addition, prolonged absorption of the injectable pharmaceutical

form may be brought about by the inclusion of agents which delay absorption such as aluminum monostearate and gelatin.

[00289] In some cases, in order to prolong the effect of a drug, it is desirable to slow the absorption of the drug from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material having poor water solubility. The rate of absorption of the drug then depends upon its rate of dissolution, which in turn, may depend upon crystal size and crystalline form.

[00290] Alternatively, delayed absorption of a parenterally-administered drug form is accomplished by dissolving or suspending the drug in an oil vehicle.

[00291] Injectable depot forms are made by forming microencapsule matrices of the subject compounds in biodegradable polymers such as polylactide-polyglycolide. Depending on the ratio of drug to polymer, and the nature of the particular polymer employed, the rate of drug release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the drug in liposomes or microemulsions, which are compatible with body tissue.

[00292] In certain embodiments, a compound or pharmaceutical preparation is administered orally. In other embodiments, the compound or pharmaceutical preparation is administered intravenously. Alternative routes of administration include sublingual, intramuscular, and transdermal administrations.

[00293] When the compounds of the present invention are administered as pharmaceuticals, to humans and animals, they can be given per se or as a pharmaceutical composition containing, for example, 0.1% to 99.5% (more preferably, 0.5% to 90%) of active ingredient in combination with a pharmaceutically acceptable carrier.

[00294] The preparations of the present invention may be given orally, parenterally, topically, or rectally. They are of course given in forms suitable for each administration route. For example, they are administered in tablets or capsule form, by injection, inhalation, eye lotion, ointment, suppository, etc. administration by injection, infusion or inhalation; topical by lotion or ointment; and rectal by suppositories. Oral administrations are preferred.

[00295] The phrases "parenteral administration" and "administered parenterally" as used herein means modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal and intrasternal injection and infusion.

[00296] The phrases "systemic administration," "administered systemically," "peripheral administration" and "administered peripherally" as used herein mean the administration of a compound, drug or other material other than directly into the central nervous system, such that it enters the patient's system and, thus, is subject to metabolism and other like processes, for example, subcutaneous administration.

[00297] These compounds may be administered to humans and other animals for therapy by any suitable route of administration, including orally, nasally, as by, for example, a spray, rectally, intravaginally, parenterally, intracisternally and topically, as by powders, ointments or drops, including buccally and sublingually.

[00298] Regardless of the route of administration selected, the compounds of the present invention, which may be used in a suitable hydrated form, and/or the pharmaceutical compositions of the present invention, are formulated into pharmaceutically-acceptable dosage forms by conventional methods known to those of skill in the art.

[00299] Actual dosage levels of the active ingredients in the pharmaceutical compositions of this invention may be varied so as to obtain an amount of the active ingredient that is effective to achieve the desired therapeutic response for a particular patient, composition, and mode of administration, without being toxic to the patient.

[00300] The selected dosage level will depend upon a variety of factors including the activity of the particular compound of the present invention employed, or the ester, salt or amide thereof, the route of administration, the time of administration, the rate of excretion or metabolism of the particular compound being employed, the duration of the treatment, other drugs, compounds and/or materials used in combination with the particular compound employed, the age, sex, weight, condition, general health and prior medical history of the patient being treated, and like factors well known in the medical arts.

[00301] A physician or veterinarian having ordinary skill in the art can readily determine and prescribe the effective amount of the pharmaceutical composition required. For example, the physician or veterinarian could start doses of the compounds of the invention employed in the pharmaceutical composition at levels lower than that required to achieve the desired therapeutic effect and then gradually increasing the dosage until the desired effect is achieved.

[00302] In some embodiments, a compound or pharmaceutical composition of the invention is provided to a subject with a lysosomal storage disease chronically. Chronic treatments include any form of repeated administration for an extended period of time, such as repeated administrations for one or more months, between a month and a year, one or more

years, or longer. In many embodiments, a chronic treatment involves administering a compound or pharmaceutical composition of the invention repeatedly over the life of the subject. Preferred chronic treatments involve regular administrations, for example one or more times a day, one or more times a week, or one or more times a month. In general, a suitable dose such as a daily dose of a compound of the invention will be that amount of the compound that is the lowest dose effective to produce a therapeutic effect. Such an effective dose will generally depend upon the factors described above. Generally doses of the compounds of this invention for a patient, when used for the indicated effects, will range from about 0.0001 to about 100 mg per kg of body weight per day. Preferably the daily dosage will range from 0.001 to 50 mg of compound per kg of body weight, and even more preferably from 0.01 to 10 mg of compound per kg of body weight. However, lower or higher doses can be used. In some embodiments, the dose administered to a subject may be modified as the physiology of the subject changes due to age, disease progression, weight, or other factors.

[00303] If desired, the effective daily dose of the active compound may be administered as two, three, four, five, six or more sub-doses administered separately at appropriate intervals throughout the day, optionally, in unit dosage forms.

[00304] While it is possible for a compound of the present invention to be administered alone, it is preferable to administer the compound as a pharmaceutical formulation (composition) as described above.

[00305] The compounds according to the invention may be formulated for administration in any convenient way for use in human or veterinary medicine, by analogy with other pharmaceuticals. The compounds according to the invention may be formulated and/or administered to treat either the peripheral or central symptoms of lysosomal storage diseases.

[00306] According to the invention, compounds for treating neurological conditions or diseases can be formulated or administered using methods that help the compounds cross the blood-brain barrier (BBB). The vertebrate brain [and CNS] has a unique capillary system unlike that in any other organ in the body. The unique capillary system has morphologic characteristics which make up the blood-brain barrier (BBB). The blood-brain barrier acts as a system-wide cellular membrane that separates the brain interstitial space from the blood.

[00307] The unique morphologic characteristics of the brain capillaries that make up the BBB are: (a) epithelial-like high resistance tight junctions which literally cement all endothelia of brain capillaries together, and (b) scanty pinocytosis or transendothelial channels, which are abundant in endothelia of peripheral organs. Due to the unique

characteristics of the blood-brain barrier, hydrophilic drugs and peptides that readily gain access to other tissues in the body are barred from entry into the brain or their rates of entry and/or accumulation in the brain are very low.

[00308] In one aspect of the invention, farnesyl transferase inhibitor compounds that cross the BBB are particularly useful for treating the central neurological aspects of lysosomal storage diseases. In one embodiment, it is expected that farnesyl transferase inhibitors that are non-charged (*e.g.*, not positively charged) and/or non-lipophilic may cross the BBB with higher efficiency than charged (*e.g.*, positively charged) and/or lipophilic compounds. Therefore it will be appreciated by a person of ordinary skill in the art that some of the compounds of the invention might readily cross the BBB. Alternatively, the compounds of the invention can be modified, for example, by the addition of various substituents that would make them less hydrophilic and allow them to more readily cross the BBB.

[00309] Various strategies have been developed for introducing those drugs into the brain which otherwise would not cross the blood-brain barrier. Widely used strategies involve invasive procedures where the drug is delivered directly into the brain. One such procedure is the implantation of a catheter into the ventricular system to bypass the blood-brain barrier and deliver the drug directly to the brain. These procedures have been used in the treatment of brain diseases which have a predilection for the meninges, *e.g.*, leukemic involvement of the brain (US 4,902,505, incorporated herein in its entirety by reference).

[00310] Although invasive procedures for the direct delivery of drugs to the brain ventricles have experienced some success, they are limited in that they may only distribute the drug to superficial areas of the brain tissues, and not to the structures deep within the brain. Further, the invasive procedures are potentially harmful to the patient.

[00311] Other approaches to circumventing the blood-brain barrier utilize pharmacologic-based procedures involving drug latentiation or the conversion of hydrophilic drugs into lipid-soluble drugs. The majority of the latentiation approaches involve blocking the hydroxyl, carboxyl and primary amine groups on the drug to make it more lipid-soluble and therefore more easily able to cross the blood-brain barrier.

[00312] Another approach to increasing the permeability of the BBB to drugs involves the intra-arterial infusion of hypertonic substances which transiently open the blood-brain barrier to allow passage of hydrophilic drugs. However, hypertonic substances are potentially toxic and may damage the blood-brain barrier.

[00313] Peptide compositions of the invention may be administered using chimeric peptides wherein the hydrophilic peptide drug is conjugated to a transportable peptide,

capable of crossing the blood-brain barrier by transcytosis at a much higher rate than the hydrophilic peptides alone. Suitable transportable peptides include, but are not limited to, histone, insulin, transferrin, insulin-like growth factor I (IGF-I), insulin-like growth factor II (IGF-II), basic albumin and prolactin.

[00314] Antibodies are another method for delivery of compositions of the invention. For example, an antibody that is reactive with a transferrin receptor present on a brain capillary endothelial cell, can be conjugated to a neuropharmaceutical agent to produce an antibody-neuropharmaceutical agent conjugate (US 5,004,697, incorporated herein in its entirety by reference). The method is conducted under conditions whereby the antibody binds to the transferrin receptor on the brain capillary endothelial cell and the neuropharmaceutical agent is transferred across the blood brain barrier in a pharmaceutically active form. The uptake or transport of antibodies into the brain can also be greatly increased by cationizing the antibodies to form cationized antibodies having an isoelectric point of between about 8.0 to 11.0 (US 5,527,527, incorporated herein in its entirety by reference).

[00315] A ligand-neuropharmaceutical agent fusion protein is another method useful for delivery of compositions to a host (US 5,977,307, incorporated herein in its entirety by reference). The ligand is reactive with a brain capillary endothelial cell receptor. The method is conducted under conditions whereby the ligand binds to the receptor on a brain capillary endothelial cell and the neuropharmaceutical agent is transferred across the blood brain barrier in a pharmaceutically active form. In some embodiments, a ligand-neuropharmaceutical agent fusion protein, which has both ligand binding and neuropharmaceutical characteristics, can be produced as a contiguous protein by using genetic engineering techniques. Gene constructs can be prepared comprising DNA encoding the ligand fused to DNA encoding the protein, polypeptide or peptide to be delivered across the blood brain barrier. The ligand coding sequence and the agent coding sequence are inserted in the expression vectors in a suitable manner for proper expression of the desired fusion protein. The gene fusion is expressed as a contiguous protein molecule containing both a ligand portion and a neuropharmaceutical agent portion.

[00316] The permeability of the blood brain barrier can be increased by administering a blood brain barrier agonist, for example bradykinin (US 5,112,596, incorporated herein in its entirety by reference), or polypeptides called receptor mediated permeabilizers (RMP) (US 5,268,164, incorporated herein in its entirety by reference). Exogenous molecules can be administered to the host's bloodstream parenterally by subcutaneous, intravenous or intramuscular injection or by absorption through a bodily tissue, such as the digestive tract,

the respiratory system or the skin. The form in which the molecule is administered (e.g., capsule, tablet, solution, emulsion) depends, at least in part, on the route by which it is administered. The administration of the exogenous molecule to the host's bloodstream and the intravenous injection of the agonist of blood-brain barrier permeability can occur simultaneously or sequentially in time. For example, a therapeutic drug can be administered orally in tablet form while the intravenous administration of an agonist of blood-brain barrier permeability is given later (e.g., between 30 minutes later and several hours later). This allows time for the drug to be absorbed in the gastrointestinal tract and taken up by the bloodstream before the agonist is given to increase the permeability of the blood-brain barrier to the drug. On the other hand, an agonist of blood-brain barrier permeability (e.g., bradykinin) can be administered before or at the same time as an intravenous injection of a drug. Thus, the term "co-administration" is used herein to mean that the agonist of blood-brain barrier and the exogenous molecule will be administered at times that will achieve significant concentrations in the blood for producing the simultaneous effects of increasing the permeability of the blood-brain barrier and allowing the maximum passage of the exogenous molecule from the blood to the cells of the central nervous system.

[00317] In other embodiments, compounds of the invention can be formulated as a prodrug with a fatty acid carrier (and optionally with another neuroactive drug). The prodrug is stable in the environment of both the stomach and the bloodstream and may be delivered by ingestion. The prodrug passes readily through the blood brain barrier. The prodrug preferably has a brain penetration index of at least two times the brain penetration index of the drug alone. Once in the central nervous system, the prodrug, which preferably is inactive, is hydrolyzed into the fatty acid carrier and the farnesyl transferase inhibitor (and optionally another drug). The carrier preferably is a normal component of the central nervous system and is inactive and harmless. The compound and/or drug, once released from the fatty acid carrier, is active. Preferably, the fatty acid carrier is a partially-saturated straight chain molecule having between about 16 and 26 carbon atoms, and more preferably 20 and 24 carbon atoms. Examples of fatty acid carriers are provided in US Patents. 4,939,174; 4,933,324; 5,994,932; 6,107,499; 6,258,836; and 6,407,137, the disclosures of which are incorporated herein by reference in their entirety.

[00318] The administration of the agents of the present invention may be for either prophylactic or therapeutic purposes. When provided prophylactically, the agent is provided in advance of disease symptoms. The prophylactic administration of the agent serves to prevent or reduce the rate of onset of symptoms of a lysosomal storage disease. When

provided therapeutically, the agent is provided at (or shortly after) the onset of the appearance of symptoms of actual disease. In some embodiments, the therapeutic administration of the agent serves to reduce the severity and duration of the disease.

[00319] The function and advantage of these and other embodiments of the present invention will be more fully understood from the examples described below. The following examples are intended to illustrate the benefits of the present invention, but do not exemplify the full scope of the invention.

Examples

Experimental Procedures

[00320] Tissue culture: All cell lines were obtained by ATCC. SH-SY5Y and Cos-7 were grown in 10% FBS DMEM (Sigma). Cells were split the day before experiments including transfection, metabolic labeling and drug treatment.

[00321] Proteins and antibodies: UCH-L1 variants were purified according to the published procedure. Actin antibody and FLAG antibody (M2) were from Sigma. UCH-L1 antibody (anti-PGP 9.5) was from Chemicon.

[00322] Chemicals: FTI-277 and lactacystin was purchased from Calbiochem. Crosslinking reagent DE was from Pierce. DMEM and MEM were purchased from Gibco. All the other material was purchased from Sigma.

[00323] Plasmids: C220S cDNA was generated by PCR site-specific mutagenesis. For the PCR, the 5' primer is uchforw SEQ ID NO: 1

(CTAAAGCTTATGCAGCTCAAGCCGATGGAG), and 3' primer is uchc220s SEQ ID NO:2 (CTAAGA CTCGAGTTAGGCTGCCTTGCTGAGAGC). Wt UCH-L1 served as the

template. The PCR fragment was inserted into pcDNA vector. For S18YC220S mutant, S18Y UCH-L1 served as the template in PCR. For the FLAG tagged UCH-L1, the 5' primer is FLAGuchforw SEQ ID NO: 3

(CTAAAGCTTATGGACTACAAGGATGACGACGACAAAGATGCAGCTCAAGC CGATGGAG), and the 3' primer is uchrev SEQ ID NO: 4

(ATCCTCGAGTTAGGCTGCCTTGACGAGAGC). Wt UCH-L1 or C220S served as the template. PCR fragment was purified and inserted into pcDNA vector. For the FLAG tagged UCH-L3, the 5' primer is L3HindIII SEQ ID NO: 5 (CTAAAGCTTATGGACTAC AAGGATGACGACGACAAAGATGGAGGGTCAACGCTGGCTG), the 3' primer is L3XhoISAA SEQ ID NO: 6 (ATCCTCGAGCTATGCTGCAGAAAGAGCAATCGCA).

For the UCH-L3 CKAA variant, the 5' primer is L3 HindIII and the 3' primer is L3XhoICKAA SEQ ID NO: 7

(ATCCTCGAGCTATGCTGCCTTAGAAAGAGCAATCGCATTAAATC).

α -synuclein degradation assay: Lipofectamine 2000 was used to transfect COS-7 cells according to the Invitrogen protocol. Transfected cells were cultured at 37 °C for 48 hours before being treated with 35 μ M lactacystin or DMSO. After 24 hours of incubation, the cells were lysed with Tris buffer (50 mM Tris, 2% SDS, 0.1% NP-40), and subjected to SDS-PAGE, followed by quantitative Western blotting.

[00324] Salt and detergent treatment of SV fraction: SV fraction was prepared as described elsewhere. SV was incubated with various salts at designed concentration for 30 minutes on ice, or 1% Triton X-100 or control without salts and detergent. Treated SV was pelleted at 100,000g for 30 minutes. Supernatants and pellets were subjected to SDS-PAGE and Western blotting.

[00325] Membrane fractionation: Cells were harvested by scraping and washed with PBS. Cell pellet was suspended in lysis buffer (50 mM Tris-HCl, 1 mM EDTA) supplemented with protease inhibitor cocktail (Sigma) and homogenized by passing through 26G needles 10 times. Suspension was clarified by spinning at 600g for 5 minutes. Clarified suspension was ultracentrifuged at 100,000g for 2 hours and separated into membrane and cytosol. Membrane fraction was washed with washing buffer (50 mM Tris-HCl, 1 mM EDTA 1 M NaCl), and pelleted each time with bench-top centrifuge.

[00326] 2D electrophoresis: For the isolation of total cellular protein, cultured SH-SY5Y cells maintained as described above were rinsed with ice-cold PBS. Cells were lysed in 1ml dSDS buffer (50mM Tris-HCl, pH 8.0 0.1% SDS) supplemented with protease inhibitor cocktail. Lysates were boiled for 3 min, and were treated with Dnase and Rnase as described. Lysates were precipitated with ice-cold acetone for at least 2 hours, and pellets were resuspended in 2D sample buffer (8M urea, 0.5% CHAPS, 0.2% DTT, 0.5% IPG buffer, 0.002% bromophenol blue). 2D electrophoresis was carried out according to manufacture's protocol (Amersham Life Science). 7cm pH 4-7 strips were used. For SH-SY5Y membrane fraction, culture SH-SY5Y cells were rinsed with cold PBS and harvested with lysis buffer (50mM Tris-HCl, pH 8.0, 1mM ZnAc₂, 250mM sucrose). Lysate was passed through 25G needles for several times and spun at 1000g for 5 min. Supernatant was centrifuged at 200,000g for 2 hours. Pellet was extensively washed with lysis buffer and extracted with cold acetone. Pellet was resuspended in 2D sample buffer.

[00327] Viral Infection: Viral infection and MTT assay in SH-SY5Y cells: The viruses were amplified and purified according to the published procedure. SH-SY5Y cells were grown on 100mm petri-dishes and induced with 100 nM retinoic acid for 3-5 days before the virus infection with M.I.O at 75. Viruses were diluted with DPBS to desired M.I.O. After four hours of incubation, 10ml growth medium was added. On the second day, cells were splitted into 96-well plates and treated with compounds for next 48 hours. The growth medium in each well was replaced with growth medium with 5 µg/ml MTT. Medium was removed after three hours incubation, and 200 µl isopropyl (0.04 N HCl) was added into each well. The signal was read at 570 nm.

[00328] Viable cell counting: At stated time poins, SH-SY5Y cells were trypsinized with 100 µl trypsin-EDTA for 1 minute and neutralized with 400 µl growth medium. Cell suspension was made up by mixing 0.2 ml of cells in growth medium, 0.3 ml of HBSS and 0.5 ml of 0.4% Trypan Blue solution. Viable cell numbers were counted by standard cell counting chamber.

[00329] Western Blotting: Following transfer of SDS gels onto NC membrane, all membranes were blocked with 5% non-fat milk in TBST (50mM Tris-HCl pH 7.4, 150mM NaCl, 0.1% Tween 20), and incubated with primary antibody overnight with 1% BSA in TBST, washed three times with TBST, and incubated with horseradish peroxidase-conjugated secondary antibody for 1 hour (Promega). Bound antibodies were detected using enhanced chemiluminascence (NEM).

Example 1: UCH-L1 is farnesylated in vivo and in cell culture

[00330] The UCH-L1 sequence contains the sequence CXXX, a consensus farnesylation site, at its C-terminus. This sequence is not present in UCH-L3. The possibility that this sequence was modified *in vivo* was investigated. First, the chemical nature of the previously reported association of UCH-L1 and synaptic vesicles from rat brain was probed.

[00331] The results are shown in *Figure 1*, panel A: Effects of various amount of salt and non-ionic detergent on the dissociations of synapsin I, synaphysin and UCH-L1 from SV was analyzed by treating aliquots of SV fraction with either KCl, NaCl, MgCl₂, or 1% Triton X-100. Membrane fraction and soluble fraction was separated by centrifugation and each fraction was subjected to SDS-PAGE followed by Western blots. a (synapsin I), c (synaphysin) and e (UCH-L1) are from pellet, and b (synapsin I), d (synaphysin) and f (UCH-L1) are supernatant fractions. Unlike synapsin (*Figure 1*, panel A, rows a and b), which is not an integral membrane protein, and like synaptophysin (rows c and d), UCH-L1 (rows e

and f) could not be separated from the vesicular fraction by increasing salt concentration. Only treatment with detergent was sufficient to solubilize UCH-L1, consistent with its farnesylation.

[00332] Analysis of various fractions from SH-SY5Y neuroblastoma cells (similar results from rat brain, not shown) by two-dimensional SDS-PAGE gel electrophoresis showed two major and two minor species in the total homogenate and one species in the membrane-associated fraction (*Figure 1*, panel B: More than 2 forms of UCH-L1 were present in SH-SY5Y cell (gel a) detected using 2D electrophoretic analysis followed by Western blotting. Only one of them (open arrow) is associated with membrane (gel b). Treatment of SH-SY5Y cells with FTI-277 (gel d) results in a significant decrease in the amount of membrane bound UCH-L1 (open arrow) without affecting the amount of cytosolic UCH-L1 (close arrow) when compared to cells treated with DMSO (gel c). This species was presumably the fully processed species: farnesylated, truncated and C-terminally methylated.

[00333] Consistent with this premise, treatment of the cells with the farnesyl transferase inhibitor FTI-277 decreased the amount of the membrane-associated species. In addition, a UCH-L1-containing species was immunoprecipitated from whole cell lysate by an anti-farnesyl antibody (Calbiochem). Finally, treatment of the cells with ^{14}C -mevalonic acid or with ^3H -farnesol resulted in incorporation of radiolabel into UCH-L1 (*Figure 1*, panel C). UCH-L1 was modified with ^{14}C mevalonate (gel a) and ^3H farnesol (gel b) *in vivo*. (b). Transfection of the C220S mutant into COS-7 cells prevented radioincorporation and eliminated the membrane-associated species (not shown). *Figure 1*, panel D, shows that WT UCH-L1 but not the C220S variant was detected in the membrane fraction of COS-7 cells transfected with either of the UCH-L1 variants).

Example 2: Removal of the farnesylation site has no effect on the *in vitro* enzymatic activity or aggregation properties of UCH-L1

[00334] The C220S mutant as expressed in *E. coli* and purified using a published method. As expected from examination of structural models of UCH-L1, the point mutation had no effect on the *in vitro* hydrolase (*Figure 2*, panel A) or ligase (panel B) activities. (A) Michaelis-Menten plot of various amount Ub-AMC titrated against either UCH-L1 WT (close circle) or C220S (open circle) showed comparable hydrolytic activities. (B) The mutation does not affect UCH-L1 *in vitro* ligase activity. In addition, the C220S mutation did not eliminate the propensity of S18 to oligomerize. This finding cleared the way to examine the effects of C220S in cell culture.

[00335] The commercially-available small molecule farnesyl transferase inhibitor FTI-277, which had previously been shown to reduce the amount of membrane-associated, farnesylated species (*Figure 1*, panel B, row d). This effect was eliminated by co-administration of the small-molecule UCH-L1 inhibitor (not shown), suggesting that the FTI effect was primarily due to its effect on UCH-L1. Treatment with FTI-277 reduced the total amount of UCH-L1 in SH-SY5Y cells and increased its rate of turnover (pulse-chase experiment not shown), in addition to reducing the amount of membrane-associated protein.

Example 3: Effect of LNK-754, Zarnestra, and Rapamycin in SHSY-5Y Cells

[00336] SHSY-5Y cells were plated at a density of 50,000 cells/cm² in a 8-well chamber slide for immunohistochemistry or a 12-well plate for mRNA analysis. Cells were grown at 37 °C 5% CO₂ until 70% confluence and then differentiated with 10 µM retinoic acid for 3 days. Cells were then treated with LNK-754 (10 pM-100 nM) or Zarnestra (100 nM) or rapamycin (10 µM) for 72 hours.

[00337] For the immunohistochemical analysis, cells were fixed with 4% paraformaldehyde and then permeabilized with 0.1% Triton-X and then incubated with a polyclonal anti-LC-3 antibody (1:200) (Novus) for 1 hour at RT followed by incubation with an Alexa-Fluor 568 (1:400) (Invitrogen) secondary 1 hour at room temperature and then mounted using Prolong Gold with DAPI reagent (Invitrogen). Images in *Figure 3* (top panel) were captured with a CCD camera using axiocam software (Zeiss) on a Zeiss axiovert 200 inverted fluorescent microscope at 600x magnification.

[00338] For the mRNA analysis, cells were lysed with 0.5 ml Tri reagent (Sigma) and transferred to an Eppendorf tube. Chloroform (100 µl) was added to each tube and shaken for 15 sec. Tubes were centrifuged at 12000 g for 15 min at 4 °C and the aqueous phase was transferred to a fresh tube. Isopropanol (200 µl) was added to each tube and then shaken for 15 sec. Tubes were centrifuged at 12000 g for 10 min at 4 °C and pellet was saved. After one was with 75% ethanol the pellet was air dried for 10 min and resuspended in 10 µL dH₂O. RNA quality was determined by spectrophotometry after which 1 µg RNA was used to generate a cDNA using iscript cDNA synthesis kit (Bio-Rad). For Real-Time quantitative PCR (RT-qPCR) 200 ng of sample cDNA was used for amplification with iQ SYBR green supermix (Bio-Rad) using the MyiQ single-color Real-Time PCR detection System (Bio-Rad). Primers for human LC-3 (5'-GCTACAAGGGTGAGAAGCAG and 3'-CTTGACTCAGAAGCCGAAGG) and human GAPDH (5'-

AACGGATTTGGTCGTATTGG and 3'-GCTCCTGGAAGATGGTGATG) were used in the RT-qPCR reaction. A standard curve for determining the relative amount of mRNA per sample was calculated by using known concentrations of cDNA from differentiated SHSY-5Y cells as a standard curve. LC-3 mRNA levels were normalized with GAPDH mRNA levels in the analysis (*Figure 3* (Bottom panel)). Significance was determined by T-test with $p < 0.05$.

[00339] The following publications describe useful farnesyl transferase inhibitor compounds, their structural and functional analogs and compositions and related synthetic methods: WO 2003092671, WO 200307660, WO 2002028409, US 2002077301, WO 2001076693, WO 2001060815, US 2002052380, WO 2001060368, US 2002010184, WO 2001032149, WO 2001007437, WO 2001005430, US 2002136744, WO 2000070083, WO 2000059930, US 2003220241, WO 2000025789, WO 2000025788, US 6329376, WO 2000016778, WO 2000016626, WO 2000001702, US 6562823, WO 2000001691, WO 2000001678, US 6160118, WO 9909985, US 6387903, WO 9910525, WO 9910524, WO 9910523, US 6103487, US 5859012, WO 9900654, US 6060038, US 5856326, WO 9630343, WO 9854966, WO 9844797, WO 9745412, WO 9738664, WO 9736889, WO 9736888, US 5919785, WO 9736587, WO 9630343; US 5925757, WO 9804549, WO 2003072549, WO 2003047586, US 6358968, US 20022119981, WO 9857970, WO 9857962, WO 9857948, US 5719148, WO 9630363, US 6576639, US 5874442, US 6143758, US 6214828, WO 9857959, WO 9723478, US 20040006087, US 20030229099, US 6358968, US 5939416, US 20020119981, US 6576639, US 6214828, US 5874442, US 6143758, US 5696121, US 5719148, US 5714609, US 5807853, US 6365588, US 20030055065, US 6242458; US 20020068742; WO 2003041658, WO 2002085819, WO 2001072721, WO 2000042849, WO 2003076660, WO 2002080895, WO 2002072085, WO 2002056884, WO 9730992, WO 9901434, US 2003162965, US 2002169313, US 2002002162, US 6537988, US 2003134846, US 2003073677, US 2003092705, US 6645966, US 6011029, US 6387926, US 6602883, US 6455523; US 6,258,824, US 6,388,092, US 6,710,209, US 6,479,513, US 6,740,757, US 6,734,308, US 6,645,982, US 6,579,887, US 6,545,020, US 6,458,800, US 6,451,812, US 6,420,387, US 6,294,552, US 6,187,786, US 6,177,432, US 6,169,096, US 6,150,377, US 6,037,350, US 5,968,952, WO 2002050058, WO 2002085364, WO 2002064142, WO 2002043733, WO 2001064252, US 2002019530, US 2002120145, US 2003212008, WO 2001064246, US 2003022918, WO 2001064226, US 2003027808, US 2003114487, US 2004192727, WO 2001064218, US 2003125326, WO 2001064217, US

2003078281, WO 2001064199, US 2003181473, WO 2001064198, US 2003050323, WO 2001064197, US 2003125268, WO 2001064196, US 2003060480, WO 2001064195, US 2003186925, WO 2001064194, US 2003100553, WO 2001062234, US 2003060450, WO 2001056552, US 2003027839, WO 2000001411, US 6545020, WO 2000001386, US 6451812, WO 9855124, US 6365600, US 2002091138, WO 9721701, US 6169096, US 6420387, WO 2002024687, US 2003199547, WO 2002024686, US 2003207887, WO 2002024683, WO 2002072574, US 6358961, WO 2003080058, WO 2003/021355, WO 2001/53289, WO 2000/47574, and WO 2000/12499; each of which is incorporated herein by reference. The disclosures of these and all patents, published patent applications, and scientific publications are incorporated herein by reference in their entirety.

[00340] Having now described some illustrative embodiments of the invention, it should be apparent to those skilled in the art that the foregoing is merely illustrative and not limiting, having been presented by way of example only. Numerous modifications and other illustrative embodiments are within the scope of one of ordinary skill in the art and are contemplated as falling within the scope of the invention. In particular, although many of the examples presented herein involve specific combinations of method acts or system elements, it should be understood that those acts and those elements may be combined in other ways to accomplish the same objectives. Acts, elements and features discussed only in connection with one embodiment are not intended to be excluded from a similar role in other embodiments. Further, for the one or more means-plus-function limitations recited in the following claims, the means are not intended to be limited to the means disclosed herein for performing the recited function, but are intended to cover in scope any means, known now or later developed, for performing the recited function. Use of ordinal terms such as “first”, “second”, “third”, *etc.*, in the claims to modify a claim element does not by itself connote any priority, precedence, or order of one claim element over another or the temporal order in which acts of a method are performed, but are used merely as labels to distinguish one claim element having a certain name from another element having a same name (but for use of the ordinal term) to distinguish the claim elements. Similarly, use of a), b), *etc.*, or i), ii), *etc.* does not by itself connote any priority, precedence, or order of steps in the claims. Similarly, the use of these terms in the specification does not by itself connote any required priority, precedence, or order.

[00341] The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope

by examples provided, since the examples are intended as a single illustration of one aspect of the invention and other functionally equivalent embodiments are within the scope of the invention. Various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims. The advantages and objects of the invention are not necessarily encompassed by each embodiment of the invention.

Claims

What is claimed is:

1. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject with a lysosomal storage disease a therapeutically effective amount of a farnesyl transferase inhibitor, or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof.
2. The method of claim 1, wherein the subject with a lysosomal storage disease has a disease selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucopolysulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanizaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknotodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.
3. The method of claim 1 or 2, wherein the subject is a human.
4. The method of claim 3, wherein the effective amount of the farnesyl transferase inhibitor or a pharmaceutically acceptable salt form thereof comprises about 10 ng/kg of body weight to about 1000 mg/kg of body weight at a frequency of administration from once a day to once a month.
5. The method of claim 1 or 2 further comprising administering to the subject an amount of one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.
6. The method of claim 5, wherein the non-farnesyl transferase inhibitor compound

comprises enzyme replacement therapy.

7. The method of claim 5, wherein the non-farnesyl transferase inhibitor compound comprises gene therapy.

8. An article of manufacture comprising packaging material and a farnesyl transferase inhibitor, or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor can be administered to a subject for treating a lysosomal storage disease.

9. The article of manufacture of claim 8, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucopolysulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanizaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknotodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

10. The article of manufacture of claim 8 or 9 further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

11. The article of manufacture of claim 10, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

12. The article of manufacture of claim 10, wherein the non-farnesyl transferase inhibitor compound comprises gene therapy.

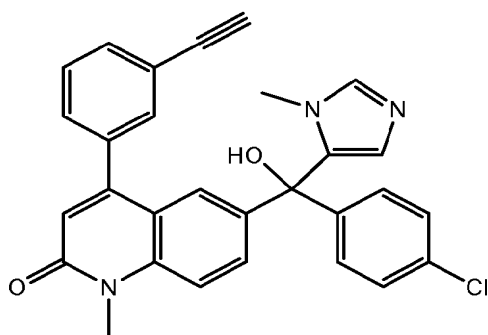
13. A pharmaceutical composition for treating a lysosomal storage disease comprising a

therapeutically effective amount of a farnesyl transferase inhibitor and a pharmaceutically acceptable excipient.

14. The pharmaceutical composition of claim 13, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

15. The pharmaceutical composition of claim 13 further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

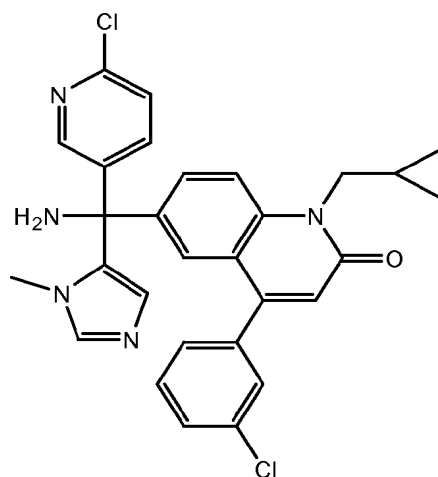
16. A method of treating a subject with a lysosomal storage disease, the method comprising, administering to a subject with a lysosomal storage disease a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof.

17. A method of treating a subject with a lysosomal storage disease, the method

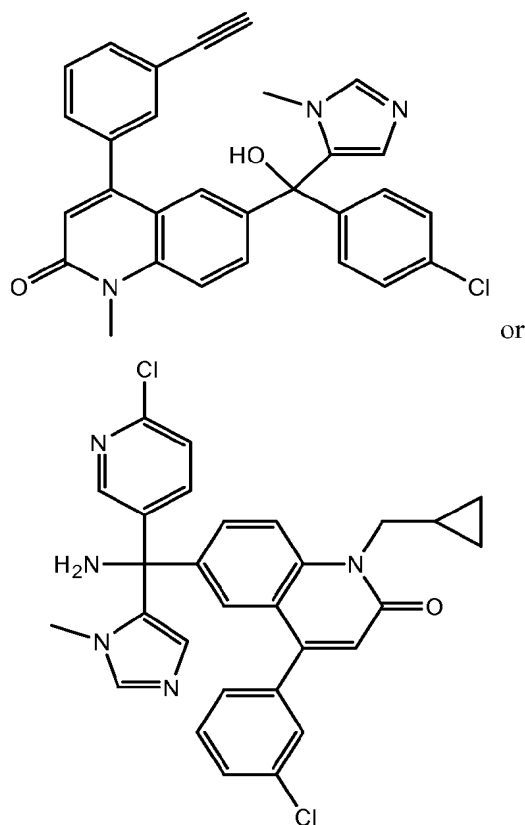
comprising, administering to a subject with a lysosomal storage disease a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof.

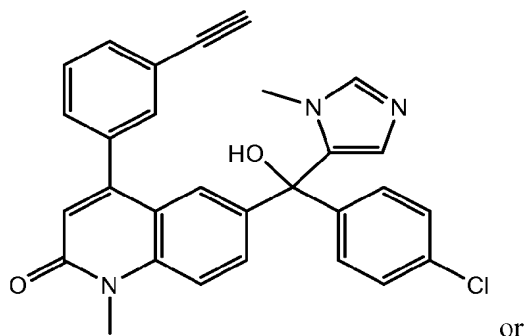
18. The method of claim 16 or 17, wherein the farnesyl transferase inhibitor is in a tartrate salt form.
19. The method of claim 16 or 17, wherein the subject with a lysosomal storage disease has a disease selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.
20. The method of claim 16 or 17, wherein the subject is a human.

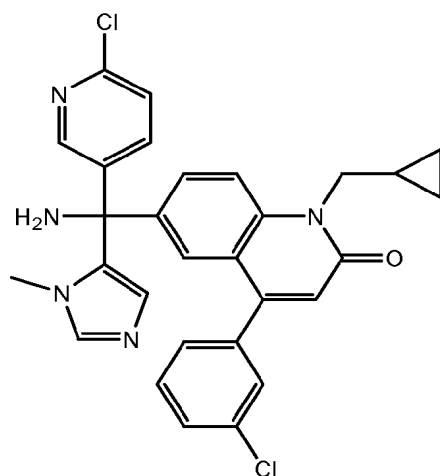
21. The method of claim 16 or 17, wherein the therapeutically effective amount comprises about 10 ng/kg of body weight to about 1000 mg/kg of body weight at a frequency of administration from once a day to once a month.
22. The method of claim 16 or 17 further comprising administering to the subject an amount of one or more non-farnesyl transferase inhibitor compounds effective in treating a lysosomal storage disease.
23. The method of claim 22, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.
24. A pharmaceutical composition for treating a subject with a lysosomal storage disease comprising a farnesyl transferase inhibitor compound of formula:



or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, and a pharmaceutically acceptable excipient.

25. The pharmaceutical composition of claim 24, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.
26. The pharmaceutical composition of claim 24, further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease
27. The pharmaceutical composition of claim 26, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.
28. An article of manufacture comprising packaging material and a farnesyl transferase inhibitor compound of formula:





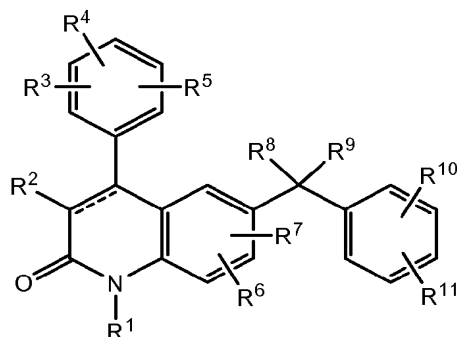
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof, wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

29. The article of manufacture of claim 28, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucopolysulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanizaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

30. The article of manufacture of claim 28 further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

31. The article of manufacture of claim 30, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

32. A method of treating a subject with a lysosomal storage disease, the method comprising, administering to a subject with a lysosomal storage disease a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



wherein

the dashed line indicates that the bond between C-3 and C-4 of the quinolin-2-one ring is a single or double bond;

R¹ is selected from H, C₁-C₁₀ alkyl, -(CR¹³R¹⁴)_qC(O)R¹², -(CR¹³R¹⁴)_qC(O)OR¹⁵, -(CR¹³R¹⁴)_qOR¹², -(CR¹³R¹⁴)_qSO₂R¹⁵, -(CR¹³R¹⁴)_t(C₃-C₁₀ cycloalkyl), -(CR¹³R¹⁴)_t(C₆-C₁₀ aryl), and -(CR¹³R¹⁴)_t(4-10 membered heterocyclic), wherein t is an integer from 0 to 5 and q is an integer from 1 to 5, said cycloalkyl, aryl and heterocyclic R¹ groups are optionally fused to a C₆-C₁₀ aryl group, a C₅-C₈ saturated cyclic group, or a 4-10 membered heterocyclic group; and the foregoing R¹ groups, except H but including any optional fused rings referred to above, are optionally substituted by 1 to 4 R⁶ groups;

R² is halo, cyano, -C(O)OR¹⁵, or a group selected from the substituents provided in the definition of R¹²;

each R³, R⁴, R⁵, R⁶, and R⁷ is independently selected from H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, halo, cyano, nitro, mercapto, trifluoromethyl, trifluoromethoxy, azido, -OR¹², -C(O)R¹², -C(O)OR¹², -NR¹³C(O)OR¹⁵, -OC(O)R¹², -NR¹³SO₂R¹⁵, -SO₂NR¹²R¹³, -NR¹³C(O)R¹², -C(O)NR¹²R¹³, -NR¹²R¹³, -CH=NOR¹², -S(O)_jR¹² wherein j is an integer from 0 to 2, -(CR¹³R¹⁴)_t(C₆-C₁₀ aryl), -(CR¹³R¹⁴)_t(4-10 membered heterocyclic), -(CR¹³R¹⁴)_t(C₃-C₁₀ cycloalkyl), and -(CR¹³R¹⁴)_tC≡CR¹⁶, and wherein in the foregoing R³, R⁴, R⁵, R⁶, and R⁷ groups t is an integer from 0 to 5; the cycloalkyl, aryl and heterocyclic moieties of the foregoing groups are optionally fused to a C₆-C₁₀ aryl group, a C₅-C₈ saturated cyclic group, or a 4-10 membered heterocyclic group; and said alkyl, alkenyl, cycloalkyl, aryl and heterocyclic groups are optionally substituted by 1 to 3 substituents independently selected

from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-\text{NR}^{13}\text{SO}_2\text{R}^{15}$, $-\text{SO}_2\text{NR}^{12}\text{R}^{13}$, $-\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{OR}^{12}$, $-\text{OC}(\text{O})\text{R}^{12}$, $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{15}$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{12}$, $-\text{C}(\text{O})\text{NR}^{12}\text{R}^{13}$, $-\text{NR}^{12}\text{R}^{13}$, $-\text{OR}^{12}$, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, $-(\text{CR}^{13}\text{R}^{14})_t(\text{C}_6\text{-C}_{10} \text{ aryl})$, and $-(\text{CR}^{13}\text{R}^{14})_t(4\text{-}10 \text{ membered heterocyclic})$, wherein t is an integer from 0 to 5;

R^8 is H, $-\text{OR}^{12}$, $-\text{NR}^{12}\text{R}^{13}$, $-\text{NR}^{12}\text{C}(\text{O})\text{R}^{13}$, cyano, $-\text{C}(\text{O})\text{OR}^{13}$, $-\text{SR}^{12}$, $-(\text{CR}^{13}\text{R}^{14})_t(4\text{-}10 \text{ membered heterocyclic})$, wherein t is an integer from 0 to 5, or $\text{C}_1\text{-C}_6$ alkyl, wherein said heterocyclic and alkyl moieties are optionally substituted by 1 to 3 R^6 substituents;

R^9 is $-(\text{CR}^{13}\text{R}^{14})_t(\text{imidazolyl})$ wherein t is an integer from 0 to 5 and said imidazolyl moiety is optionally substituted by 1 or 2 R^6 substituents;

each R^{10} and R^{11} is independently selected from the substituents provided in the definition of R^6 ;

each R^{12} is independently selected from H , $\text{C}_1\text{-C}_{10}$ alkyl, $-(\text{CR}^{13}\text{R}^{14})_t(\text{C}_3\text{-C}_{10} \text{ cycloalkyl})$, $-(\text{CR}^{13}\text{R}^{14})_t(\text{C}_6\text{-C}_{10} \text{ aryl})$, and $-(\text{CR}^{13}\text{R}^{14})_t(4\text{-}10 \text{ membered heterocyclic})$, wherein t is an integer from 0 to 5; said cycloalkyl, aryl and heterocyclic R^{12} groups are optionally fused to a $\text{C}_6\text{-C}_{10}$ aryl group, a $\text{C}_5\text{-C}_8$ saturated cyclic group, or a 4-10 membered heterocyclic group; and the foregoing R^{12} substituents, except H, are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-\text{C}(\text{O})\text{R}^{13}$, $-\text{C}(\text{O})\text{OR}^{13}$, $-\text{OC}(\text{O})\text{R}^{13}$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{14}$, $-\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$, $-\text{NR}^{13}\text{R}^{14}$, hydroxy, $\text{C}_1\text{-C}_6$ alkyl, and $\text{C}_1\text{-C}_6$ alkoxy;

each R^{13} and R^{14} is independently H or $\text{C}_1\text{-C}_6$ alkyl, and where R^{13} and R^{14} are as $-(\text{CR}^{13}\text{R}^{14})_q$ or $(\text{CR}^{13}\text{R}^{14})_t$ each is independently defined for each iteration of q or t in excess of 1;

R^{15} is selected from the substituents provided in the definition of R^{12} except R^{15} is not H;

R^{16} is selected from the list of substituents provided in the definition of R^{12} and $-\text{SiR}^{17}\text{R}^{18}\text{R}^{19}$;

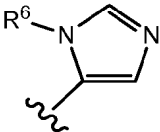
R^{17} , R^{18} and R^{19} are each independently selected from the substituents provided in the definition of R^{12} except R^{17} , R^{18} and R^{19} are not H; and

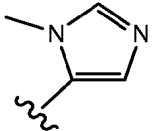
provided that at least one of R^3 , R^4 and R^5 is $-(\text{CR}^{13}\text{R}^{14})_t\text{C}\equiv\text{CR}^{16}$ wherein t is an integer from 0 to 5 and R^{13} , R^{14} , and R^{16} are as defined above;

or a derivative, analog, stereoisomer, isomer, solvate, or salt thereof.

33. The method of claim 32, wherein R^1 is methyl.

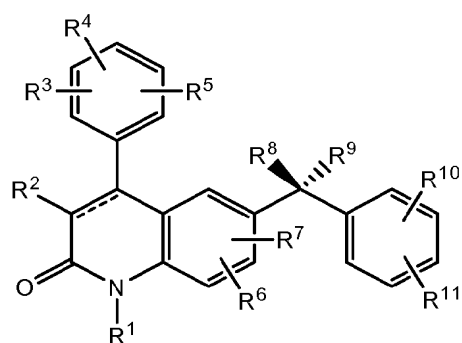
34. The method of claim 32, wherein the dotted line represents a bond.
35. The method of claim 32, wherein R^1 is hydrogen or C_{1-6} alkyl.
36. The method of claim 32, wherein R^2 is hydrogen.
37. The method of claim 32, wherein R^2 is hydrogen, a halogen, or C_1-C_6 alkyl.
38. The method of claim 32, wherein R^3 is hydrogen; R^4 is hydrogen; and R^5 is ethynyl.
39. The method of claim 32, wherein at least one of R^3 , R^4 , and R^5 is ethynyl.
40. The method of claim 32, wherein at least one of R^3 , R^4 , and R^5 is $-(CR^{13}R^{14})_nC\equiv CR^{16}$.
41. The method of claim 32, wherein R^6 is hydrogen.
42. The method of claim 32, wherein R^7 is hydrogen.
43. The method of claim 32, wherein R^8 is hydrogen, $-OR^{12}$, or $-NR^{12}R^{13}$.
44. The method of claim 32, wherein R^8 is $-OH$.
45. The method of claim 32, wherein R^8 is $-NH_2$.

46. The method of claim 32, wherein R^9 is  .

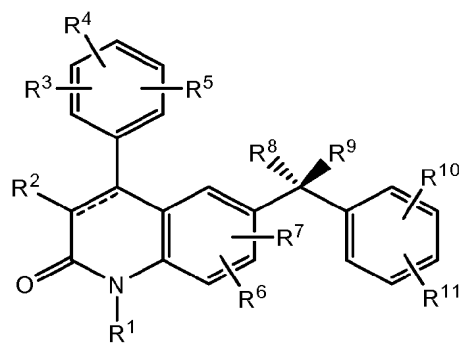
47. The method of claim 32, wherein R^9 is  .

48. The method of claim 32, wherein R^{10} is hydrogen.

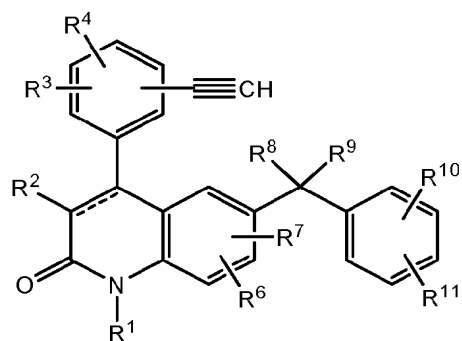
49. The method of claim 32, wherein R^{10} is halogen.
50. The method of claim 32, wherein R^{10} is chlorine.
51. The method of claim 32, wherein at least one of R^{10} and R^{11} is hydrogen.
52. The method of claim 32, wherein the compound has the stereochemistry as shown in formula:



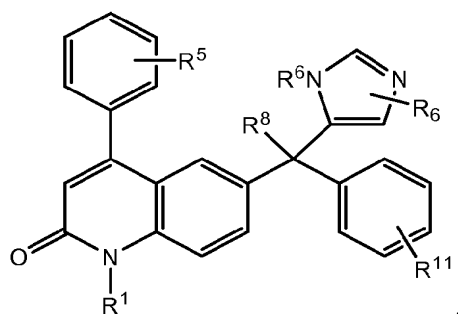
53. The method of claim 32, wherein the compound has the stereochemistry as shown in formula:



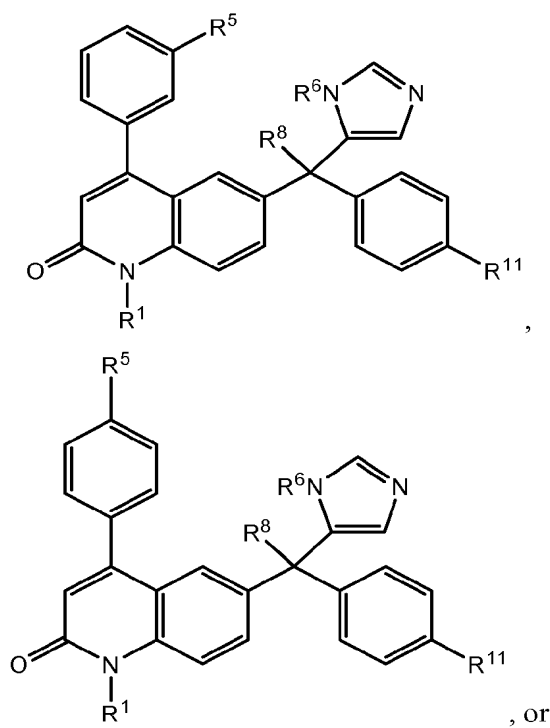
54. The method of claim 32, wherein the compound is of the formula:

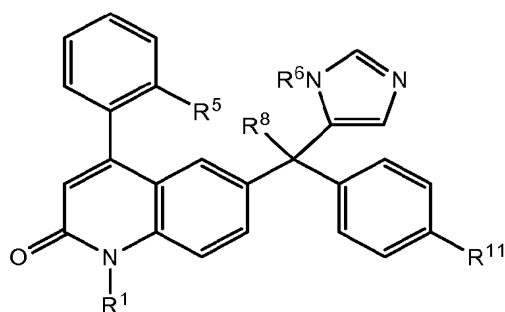


55. The method of claim 32, wherein the compound is of the formula:

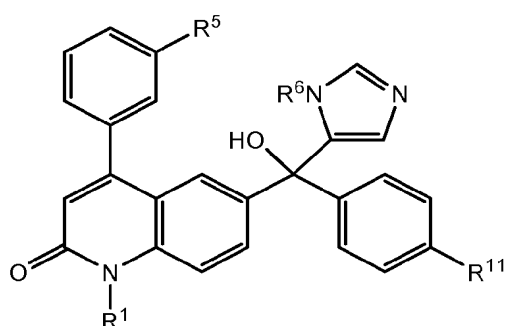


56. The method of claim 32, wherein the compound is of one of the formulae:





57. The method of claim 32, wherein the compound is of the formula:



58. The method of claim 32, wherein the subject with a lysosomal storage disease has a disease selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucopolysulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanizaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

59. The method of claim 32, wherein the subject is a human.

60. The method of claim 32, wherein the effective amount comprises about 10 ng/kg of body weight to about 1000 mg/kg of body weight at a frequency of administration from once

a day to once a month.

61. The method of claim 32, further comprising administering to the subject an amount of one or more non-farnesyl transferase inhibitor compounds effective in treating a lysosomal storage disease.

62. The method of claim 61, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

63. A pharmaceutical composition for treating a lysosomal storage disease comprising a farnesyl transferase inhibitor compound of claim 32 and a pharmaceutically acceptable excipient.

64. The pharmaceutical composition of claim 63, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

65. The pharmaceutical composition of claim 48, further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

66. An article of manufacture comprising packaging material and a farnesyl transferase inhibitor compound of claim 32 wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

67. The article of manufacture of claim 66, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucolipidosis II, mucolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

68. The article of manufacture of claim 66, further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

69. The article of manufacture of claim 68, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

70. A method of treating a subject with a lysosomal storage disease, the method comprising administering to the subject with a lysosomal storage disease a therapeutically effective amount of 6-[(4-chloro-phenyl)-hydroxy(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-ethynyl-phenyl)-1-methyl-1H-quinolin-2-one, 2,3-dihydroxy butanedioate.

71. A method of treating a subject with a lysosomal storage disease, the method comprising administering to the subject a therapeutically effective amount of 6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-cyclopropylmethyl-1H-quinolin-2-one.

72. The method of claim 70 or 71, wherein the subject has a lysosomal storage disease selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucolipidosis II, mucolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis,

fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

73. The method of claim 70 or 71, wherein the subject is a human.

74. The method of claim 70 or 71, wherein the effective amount comprises about 10 ng/kg of body weight to about 1000 mg/kg of body weight at a frequency of administration from once a day to once a month.

75. The method of claim 70 or 71, further comprising administering to the subject an amount of one or more non-farnesyl transferase inhibitor compounds effective in treating a lysosomal storage disease.

76. The method of claim 75, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

77. A pharmaceutical composition for treating a lysosomal storage disease comprising 6-[(4-chloro-phenyl)-hydroxy(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-ethynyl-phenyl)-1-methyl-1H-quinolin-2-one, 2,3-dihydroxy butanedioate and a pharmaceutically acceptable excipient.

78. A pharmaceutical composition for treating a lysosomal storage disease comprising 6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-cyclopropylmethyl-1H-quinolin-2-one and a pharmaceutically acceptable excipient.

79. The pharmaceutical composition of claim 77 or 78, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff

disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

80. The pharmaceutical composition of claim 77 or 78 further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

81. An article of manufacture comprising packaging material and 6-[(4-chloro-phenyl)-hydroxy(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-ethynyl-phenyl)-1-methyl-1H-quinolin-2-one, 2,3-dihydroxy butanedioate wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

82. An article of manufacture comprising packaging material and 6-[amino-(6-chloro-pyridin-3-yl)-(3-methyl-3H-imidazol-4-yl)-methyl]-4-(3-chloro-phenyl)-1-cyclopropylmethyl-1H-quinolin-2-one wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

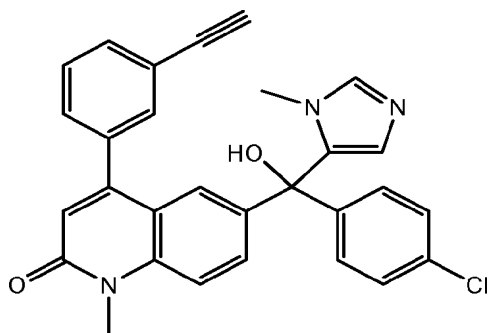
83. The article of manufacture of claim 81 or 82, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis,

neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

84. The article of manufacture of claim 81 or 82 further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

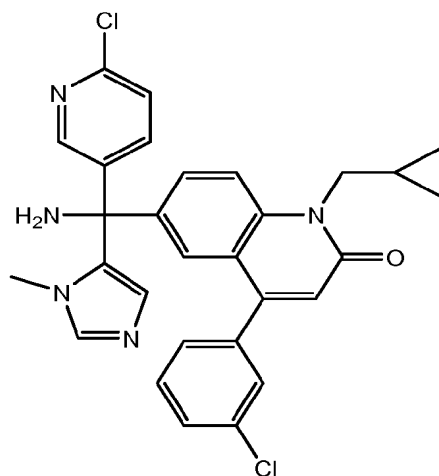
85. The article of manufacture of claim 84, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

86. A method of reducing toxicity of an accumulated substrate in a cell due to a protein deficiency, the method comprising, administering to a cell a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



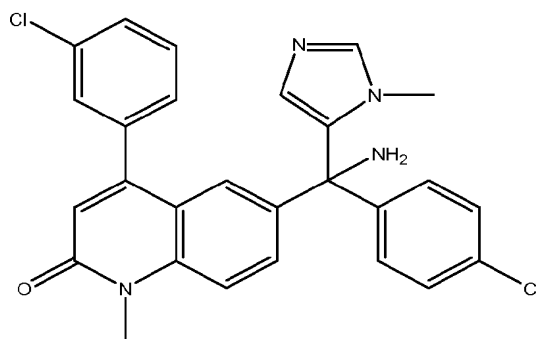
or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof.

87. A method of reducing toxicity of an accumulated substrate in a cell due to a protein deficiency, the method comprising, administering to a cell a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof.

88. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject with a lysosomal storage disease a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof.

89. The method of claim 88, wherein the subject has a lysosomal storage disease selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃

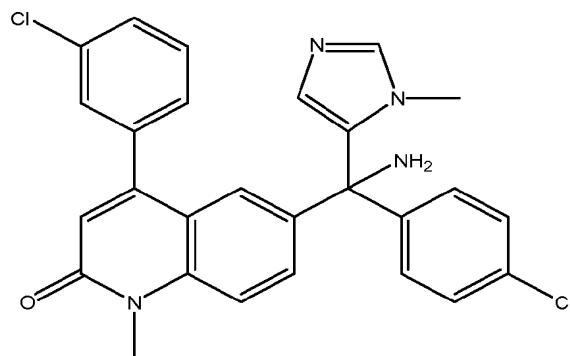
gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

90. The method of claim 88, wherein the subject is a human.

91. The method of claim 88, wherein the therapeutically effective amount comprises about 10 ng/kg of body weight to about 1000 mg/kg of body weight at a frequency of administration from once a day to once a month.

92. The method of claim 88 further comprising administering to the subject an amount of one or more non-farnesyl transferase inhibitor compounds effective in treating a lysosomal storage disease.

93. A pharmaceutical composition for treating a subject with a lysosomal storage disease comprising a farnesyl transferase inhibitor compound of formula:



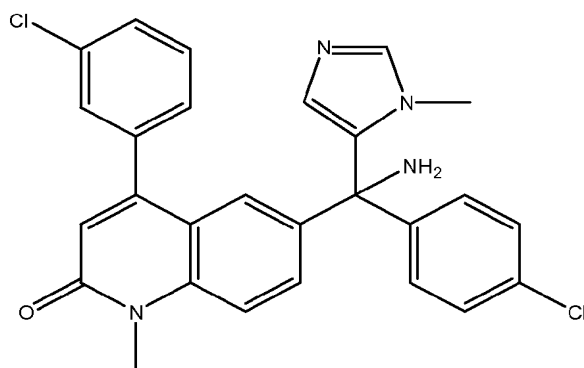
or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof; and a pharmaceutically acceptable excipient.

94. The pharmaceutical composition of claim 93, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C,

Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

95. The pharmaceutical composition of claim 93, further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

96. An article of manufacture comprising packaging material and a farnesyl transferase inhibitor compound of formula:



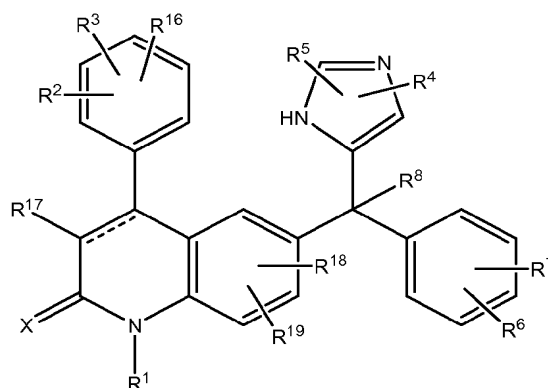
or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof; wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

97. The article of manufacture of claim 96, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucolipidosis II, mucolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis,

neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

98. The article of manufacture of claim 96 further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

99. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject with a lysosomal storage disease a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof, in a therapeutically effective amount;

wherein

the dotted line represents an optional bond;

X is oxygen or sulfur;

R¹ is hydrogen, C₁₋₁₂ alkyl, Ar¹, Ar² C₁₋₆ alkyl, quinolinyC₁₋₆ alkyl, pyridylC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl, aminoC₁₋₆ alkyl, or a radical of formula -Alk¹-C(=O)-R⁹, -Alk¹-S(O)-R⁹ or -Alk¹-S(O)₂-R⁹, wherein Alk¹ is C₁₋₆ alkanediyl,

R⁹ is hydroxy, C₁₋₆ alkyl, C₁₋₆ alkyloxy, amino, C₁₋₈ alkylamino or C₁₋₈ alkylamino substituted with C₁₋₆ alkyloxycarbonyl;

R², R³ and R¹⁶ each independently are hydrogen, hydroxy, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxy, hydroxyC₁₋₆ alkyloxy, C₁₋₆ alkyloxyC₁₋₆ alkyloxy, aminoC₁₋₆ alkyloxy, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyloxy, Ar¹, Ar² C₁₋₆ alkyl, Ar² oxy, Ar² C₁₋₆ alkyloxy, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, trihalomethyl, trihalomethoxy, C₂₋₆ alkenyl, 4,4-dimethyloxazolyl;

or when on adjacent positions R^2 and R^3 taken together may form a bivalent radical of formula



R^4 and R^5 each independently are hydrogen, halo, Ar^1 , C_{1-6} alkyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, C_{1-6} alkyloxy, C_{1-6} alkylthio, amino, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylS(O) C_{1-6} alkyl or C_{1-6} alkylS(O) $_2$ C_{1-6} alkyl;

R^6 and R^7 each independently are hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxy, Ar^2 oxy, trihalomethyl, C_{1-6} alkylthio, di(C_{1-6} alkyl)amino, or

when on adjacent positions R^6 and R^7 taken together may form a bivalent radical of formula



R^8 is hydrogen, C_{1-6} alkyl, cyano, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, cyano C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, carboxy C_{1-6} alkyl, hydroxy C_{1-6} alkyl, amino C_{1-6} alkyl, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyl, imidazolyl, halo C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, aminocarbonyl C_{1-6} alkyl, or a radical of formula



wherein

R^{10} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 , Ar^2 C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, a radical or formula $-Alk^2-OR^{13}$ or $-Alk^2-NR^{14}R^{15}$;

R^{11} is hydrogen, C_{1-12} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{12} is hydrogen, C_{1-6} alkyl, C_{1-16} alkylcarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylaminocarbonyl, Ar^1 , Ar^2 C_{1-6} alkyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, a natural amino acid, Ar^1 carbonyl, Ar^2 C_{1-6} alkylcarbonyl, aminocarbonylcarbonyl, C_{1-6} alkyloxy C_{1-6} alkylcarbonyl, hydroxy, C_{1-6} alkyloxy, aminocarbonyl, di(C_{1-6} alkyl)amino C_{1-6} alkylcarbonyl, amino, C_{1-6} alkylamino, C_{1-6} alkylcarbonylamino, or a radical of formula $-Alk^2-OR^{13}$ or $-Alk^2-NR^{14}R^{15}$;

wherein

Alk² is C₁₋₆ alkanediyl;

R¹³ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, hydroxyC₁₋₆ alkyl, Ar¹ or Ar² C₁₋₆ alkyl;

R¹⁴ is hydrogen, C₁₋₆ alkyl, Ar¹ or Ar² C₁₋₆ alkyl;

R¹⁵ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, Ar¹ or Ar² C₁₋₆ alkyl;

R¹⁷ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxycarbonyl, Ar¹ ;

R¹⁸ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkyloxy or halo;

R¹⁹ is hydrogen or C₁₋₆ alkyl;

Ar¹ is phenyl or phenyl substituted with C₁₋₆ alkyl, hydroxy, amino, C₁₋₆ alkyloxy or halo; and

Ar² is phenyl or phenyl substituted with C₁₋₆ alkyl, hydroxy, amino, C₁₋₆ alkyloxy or halo.

100. The method of claim 99, wherein X is oxygen.

101. The method of claim 99, wherein the dotted line represents a bond.

102. The method of claim 99, wherein R¹ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl or mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl.

103. The method of claim 99, wherein R³ is hydrogen and R² is halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₁₋₆ alkyloxy, trihalomethoxy or hydroxyC₁₋₆ alkyloxy.

104. The method of claim 99, wherein R⁸ is hydrogen, hydroxy, haloC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, cyanoC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, imidazolyl, or a radical of formula -NR¹¹R¹² wherein R¹¹ is hydrogen or C₁₋₁₂ alkyl and R¹² is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkyloxy, C₁₋₆ alkyloxyC₁₋₆ alkylcarbonyl, hydroxy, or a radical of formula -Alk²-OR¹³ wherein R¹³ is hydrogen or C₁₋₆ alkyl.

105. The method of claim 99, wherein the compound is selected from the group consisting of:

6-[amino(4-chlorophenyl)-1-methyl-1H-imidazol-5-ylmethyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone;

4-(3-chlorophenyl)-6-[(4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl]-

1-methyl-2(1H)-quinolinone,

6-[(4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-ethoxyphenyl)-1-methyl-2(1H)-quinolinone;

6-[(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-ethoxyphenyl)-1-methyl-2(1H)-quinolinone monohydrochloride monohydrate;

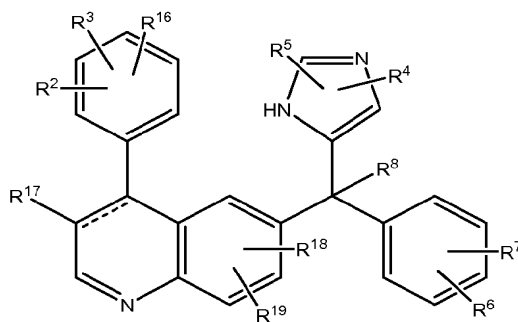
6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-ethoxyphenyl)-1-methyl-2(1H)-quinolinone,

6-amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl-1-methyl-4-(3-propylphenyl)-2(1H)-quinolinone; and

pharmaceutically acceptable stereoisomers, isomers, solvates, and salts thereof.

106. The method of claim 99, wherein the compound is (B)-6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone; or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof.

107. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof;

wherein R^2 , R^3 and R^{16} each independently are hydrogen, hydroxy, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxy, hydroxy C_{1-6} alkyloxy, C_{1-6} alkyloxy C_{1-6} alkyloxy, amino C_{1-6} alkyloxy, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyloxy, Ar^1 , Ar^2 C_{1-6} alkyl, Ar^2 oxy, Ar^2 C_{1-6} alkyloxy, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, trihalomethyl, trihalomethoxy, C_{2-6} alkenyl, 4,4-dimethyloxazolyl; or

when on adjacent positions R^2 and R^3 taken together may form a bivalent radical of formula:



- O-CH₂-CH₂-O- (a-2),
 -O-CH=CH- (a-3),
 -O-CH₂-CH₂- (a-4),
 -O-CH₂-CH₂-CH₂- (a-5), or
 -CH=CH-CH=CH- (a-6);

R⁴ and R⁵ each independently are hydrogen, halo, Ar¹, C₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkyloxy, C₁₋₆ alkylthio, amino, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl;

R⁶ and R⁷ each independently are hydrogen, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxy, Ar² oxy, trihalomethyl, C₁₋₆ alkylthio, di (C₁₋₆ alkyl) amino, or

when on adjacent positions R⁶ and R⁷ taken together may form a bivalent radical of formula

- O-CH₂-O- (c-1), or
 -CH=CH-CH=CH- (c-2);

R⁸ is hydrogen, C₁₋₆ alkyl, cyano, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, cyanoC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, carboxyC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, aminoC₁₋₆ alkyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl, imidazolyl, haloC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, aminocarbonylC₁₋₆ alkyl, or a radical of formula

- O-R¹⁰ (b-1),
 -S-R¹⁰ (b-2),
 -NR¹¹R¹² (b-3),

wherein

R¹⁰ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, Ar¹, Ar² C₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, a radical or formula -Alk² -OR¹³ or -Alk² -NR¹⁴ R¹⁵ ;

R¹¹ is hydrogen, C₁₋₁₂ alkyl, Ar¹ or Ar² C₁₋₆ alkyl;

R¹² is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylaminocarbonyl, Ar¹, Ar² C₁₋₆ alkyl, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, a natural amino acid, Ar¹ carbonyl, Ar² C₁₋₆ alkylcarbonyl, aminocarbonylcarbonyl, C₁₋₆ alkyloxyC₁₋₆ alkylcarbonyl, hydroxy, C₁₋₆ alkyloxy, aminocarbonyl, di(C₁₋₆ alkyl) aminoC₁₋₆ alkylcarbonyl, amino, C₁₋₆ alkylamino, C₁₋₆ alkylcarbonylamino, or a radical of formula -Alk² -OR¹³ or -Alk² -NR¹⁴ R¹⁵ ;

wherein Alk² is C₁₋₆ alkanediyl;

R¹³ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, hydroxyC₁₋₆ alkyl, Ar¹ or Ar² C₁₋₆ alkyl;

R^{14} is hydrogen, C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

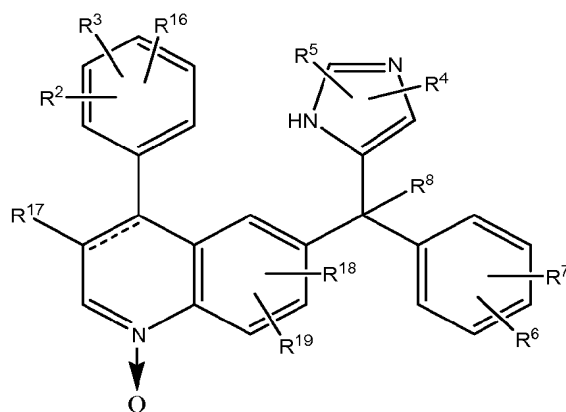
R^{15} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{17} is hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, Ar^1 ;

R^{18} is hydrogen, C_{1-6} alkyl, C_{16} alkyloxy or halo; and

R^{19} is hydrogen or C_{1-6} alkyl.

108. A method of treating a subject with a lysosomal storage disease, the method comprising administering to the subject with a lysosomal storage disease a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof,

wherein R^2 , R^3 and R^{16} each independently are hydrogen, hydroxy, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxy, hydroxy C_{1-6} alkyloxy, C_{1-6} alkyloxy C_{1-6} alkyloxy, amino C_{1-6} alkyloxy, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyloxy, Ar^1 , Ar^2 C_{1-6} alkyl, Ar^2 oxy, Ar^2 C_{1-6} alkyloxy, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, trihalomethyl, trihalomethoxy, C_{2-6} alkenyl, 4,4-dimethyloxazoly; or

when on adjacent positions R^2 and R^3 taken together may form a bivalent radical of formula:



R^4 and R^5 each independently are hydrogen, halo, Ar^1 , C_{1-6} alkyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, C_{1-6} alkyloxy, C_{1-6} alkylthio, amino, hydroxycarbonyl, C_{1-6}

alkyloxycarbonyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl;

R⁶ and R⁷ each independently are hydrogen, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxy, Ar² oxy, trihalomethyl, C₁₋₆ alkylthio, di (C₁₋₆ alkyl) amino, or

when on adjacent positions R⁶ and R⁷ taken together may form a bivalent radical of formula

-O-CH₂-O- (c-1), or

-CH=CH-CH=CH- (c-2);

R⁸ is hydrogen, C₁₋₆ alkyl, cyano, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, cyanoC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, carboxyC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, aminoC₁₋₆ alkyl, mono- or di (C₁₋₆ alkyl)aminoC₁₋₆ alkyl, imidazolyl, haloC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, aminocarbonylC₁₋₆ alkyl, or a radical of formula

-O-R¹⁰ (b-1),

-S-R¹⁰ (b-2),

-N-R¹¹ R¹² (b-3),

wherein

R¹⁰ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, Ar¹, Ar² C₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, a radical or formula -Alk² -OR¹³ or -Alk² -NR¹⁴ R¹⁵ ;

R¹¹ is hydrogen, C₁₋₁₂ alkyl, Ar¹ or Ar² C₁₋₆ alkyl;

R¹² is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylaminocarbonyl, Ar¹, Ar² C₁₋₆ alkyl, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, a natural amino acid, Ar¹ carbonyl, Ar² C₁₋₆ alkylcarbonyl, aminocarbonylcarbonyl, C₁₋₆ alkyloxyC₁₋₆ alkylcarbonyl, hydroxy, C₁₋₆ alkyloxy, aminocarbonyl, di(C₁₋₆ alkyl)aminoC₁₋₆ alkylcarbonyl, amino, C₁₋₆ alkylamino, C₁₋₆ alkylcarbonylamino, or a radical of formula -Alk² -OR¹³ or -Alk² -NR¹⁴ R¹⁵ ;

wherein

Alk² is C₁₋₆ alkanediyl;

R¹³ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, hydroxyC₁₋₆ alkyl, Ar¹ or Ar² C₁₋₆ alkyl;

R¹⁴ is hydrogen, C₁₋₆ alkyl, Ar¹ or Ar² C₁₋₆ alkyl;

R¹⁵ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, Ar¹ or Ar² C₁₋₆ alkyl;

R¹⁷ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxycarbonyl, Ar¹ ;

R¹⁸ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkyloxy or halo;

R¹⁹ is hydrogen or C₁₋₆ alkyl.

109. The method of any of claims 99-108 wherein the effective amount comprises about 10

ng/kg of body weight to about 1000 mg/kg of body weight at a frequency of administration from once a day to once a month.

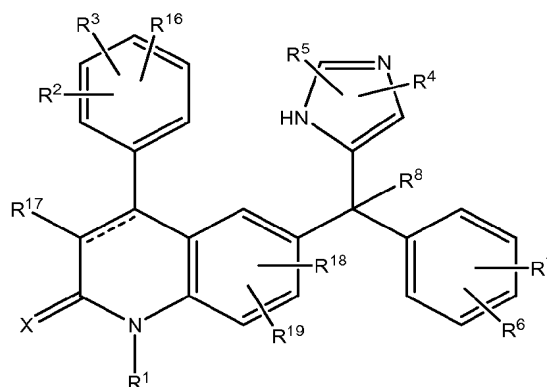
110. The method of any one of claims 99-108, further comprising administering to the subject an amount of one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

111. An article of manufacture comprising packaging material and an farnesyl transferase inhibitor compound according to any one of claims 99-108, wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

112. The article of manufacture of claim 111, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucopolysulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanizaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknotodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

113. The article of manufacture of claim 111, further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

114. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject with a lysosomal storage disease therapeutically effective amount of a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof,

wherein the dotted line represents an optional bond;

X is oxygen or sulfur;

R¹ is hydrogen, C₁₋₁₂ alkyl, Ar¹, Ar² C₁₋₆ alkyl, quinolinylC₁₋₆ -alkyl, pyridylC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl, aminoC₁₋₆ alkyl, or a radical of formula -Alk¹ -C(=O)-R⁹, -Alk¹ -S(O)-R⁹ or -Alk¹ -S(O)₂ -R⁹, wherein Alk¹ is C₁₋₆ alkanediyl,

R⁹ is hydroxy, C₁₋₆ alkyl, C₁₋₆ alkyloxy, amino, C₁₋₈ alkylamino or C₁₋₈ alkylamino substituted with C₁₋₆ alkyloxycarbonyl;

R², R³ and R¹⁶ each independently are hydrogen, hydroxy, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxy, hydroxyC₁₋₆ alkyloxy, C₁₋₆ alkyloxyC₁₋₆ alkyloxy, aminoC₁₋₆ alkyloxy, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyloxy, Ar¹, Ar² C₁₋₆ alkyl, Ar² oxy, Ar² C₁₋₆ alkyloxy, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, trihalomethyl, trihalomethoxy, C₂₋₆ alkenyl, 4,4-dimethyloxazolyl; or

when on adjacent positions R² and R³ taken together may form a bivalent radical of formula

- | | |
|--|-----------|
| -O-CH ₂ -O- | (a-1), |
| -O-CH ₂ -CH ₂ -O- | (a-2), |
| -O-CH=CH- | (a-3), |
| -O-CH ₂ -CH ₂ - | (a-4), |
| -O-CH ₂ -CH ₂ -CH ₂ - | (a-5), or |
| -CH=CH-CH=CH- | (a-6); |

R⁴ is hydrogen or C₁₋₆ alkyl;

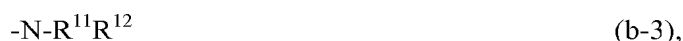
R⁵ is hydrogen;

R⁶ and R⁷ each independently are hydrogen, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxy, Ar² oxy, trihalomethyl, C₁₋₆ alkylthio, di(C₁₋₆ alkyl)amino, or

when on adjacent positions R^6 and R^7 taken together may form a bivalent radical of formula:



R^8 is hydrogen, C_{1-6} alkyl, cyano, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyl, cyano C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, carboxy C_{1-6} alkyl, hydroxy C_{1-6} alkyl, amino C_{1-6} alkyl, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyl, imidazolyl, halo C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, aminocarbonyl C_{1-6} alkyl, or a radical of formula:



wherein R^{10} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 , Ar^2 C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, a radical or formula $--Alk^2--OR^{13}$ or $--Alk^2--NR^{14}R^{15}$;

R^{11} is hydrogen, C_{1-12} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{12} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylaminocarbonyl, Ar^1 , Ar^2 C_{1-6} alkyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, a natural amino acid, Ar^1 carbonyl, Ar^2 C_{1-6} alkylcarbonyl, aminocarbonylcarbonyl, C_{1-6} alkyloxy C_{1-6} alkylcarbonyl, hydroxy, C_{1-6} alkyloxy, aminocarbonyl, di(C_{1-6} alkyl) amino C_{1-6} alkylcarbonyl, amino, C_{1-6} alkylamino, C_{1-6} alkylcarbonylamino, or a radical of formula $-Alk^2-OR^{13}$ or $-Alk^2-NR^{14}R^{15}$;

wherein Alk^2 is C_{1-6} alkanediyl;

R^{13} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, hydroxy C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{14} is hydrogen, C_{1-6} alkyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{15} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 or Ar^2 C_{1-6} alkyl;

R^{17} is hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, Ar^1 ;

R^{18} is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy or halo;

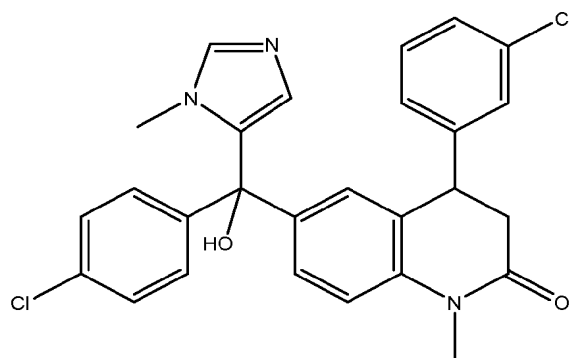
R^{19} is hydrogen or C_{1-6} alkyl;

Ar^1 is phenyl or phenyl substituted with C_{1-6} alkyl, hydroxy, amino, C_{1-6} alkyloxy or halo; and

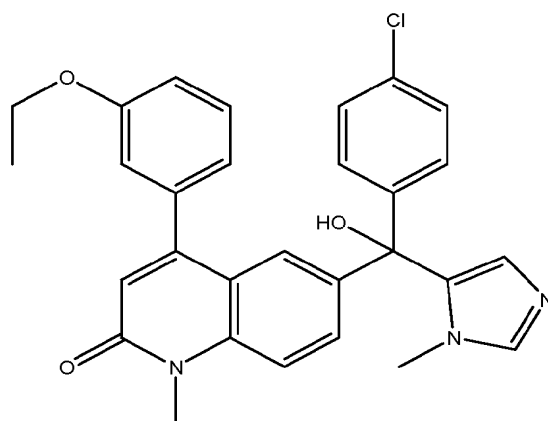
Ar^2 is phenyl or phenyl substituted with C_{1-6} alkyl, hydroxy, amino, C_{1-6} alkyloxy or halo.

115. The method of claim 114, wherein X is oxygen.

116. The method of claim 114, wherein R^6 is C_{1-6} alkyl or halo; and R^7 is hydrogen.
117. The method of claim 114, wherein
 R^1 is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, di(C_{1-6} alkyl)amino C_{1-6} alkyl, or a radical of formula $--Alk^1--C(=O)--R^9$, wherein Alk^1 is methylene and R^9 is C_{1-8} alkylamino substituted with C_{1-6} alkyloxycarbonyl;
 R^2 is halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkyloxy, trihalomethoxy, hydroxy C_{1-6} alkyloxy or Ar^1 ;
 R^3 is hydrogen;
 R^4 is methyl bound to the nitrogen in 3-position of the imidazole;
 R^5 is hydrogen;
 R^6 is chloro;
 R^7 is hydrogen;
 R^8 is hydrogen, hydroxy, halo C_{1-6} alkyl, hydroxy C_{1-6} alkyl, cyano C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, imidazolyl, or a radical of formula $--NR^{11}R^{12}$ wherein R^{11} is hydrogen or C_{1-12} alkyl and R^{12} is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy, C_{1-6} alkyloxy C_{1-6} alkylcarbonyl, or a radical of formula $--Alk^2--OR^{13}$ wherein R^{13} is C_{1-6} alkyl;
 R^{17} is hydrogen; and
 R^{18} is hydrogen.
118. The method of claim 114, wherein the farnesyl transferase inhibitor is selected from the group consisting of:



or



or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof.

119. The method of any of claims 114-118 wherein the therapeutically effective amount comprises about 10 ng/kg of body weight to about 1000 mg/kg of body weight at a frequency of administration from once a day to once a month.

120. The method of claim 119, further comprising administering to the subject an amount of one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

121. An article of manufacture comprising packaging material and a farnesyl transferase inhibitor compound according to any of claims 114-118 wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

122. The article of manufacture of claim 121, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis,

neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

123. The article of manufacture of claim 121 further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

124. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject with a lysosomal storage disease a therapeutically effective amount of a farnesyl transferase inhibitor that is an enantiomer of 6-(amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl)-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone having an α_D^{20} value of +22.86° (c=49.22 mg/5 ml, methanol) or a pharmaceutically acceptable salt thereof.

125. The method of claim 124 wherein the therapeutically effective amount comprises about 10 ng/kg of body weight to about 1000 mg/kg of body weight at a frequency of administration from once a day to once a month.

126. The method of claim 124, further comprising administering to the subject an amount of one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

127. The method of claim 126, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

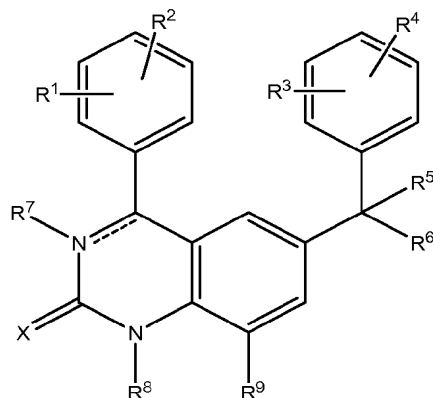
128. An article of manufacture comprising packaging material and a farnesyl transferase inhibitor compound according to claim 41, wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

129. The article of manufacture of claim 128, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolidosis II, mucopolidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis,

fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

130. The article of manufacture of claim 128 further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

131. A method of treating a subject with a lysosomal storage disease, the method comprising, administering to a subject with a lysosomal storage disease a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof, wherein

the dotted line represents an optional bond;

X is oxygen or sulfur;

R¹ and R² each independently are hydrogen, hydroxy, halo, cyano, C₁₋₆ alkyl, trihalomethyl, trihalomethoxy, C₂₋₆ alkenyl, C₁₋₆ alkyloxy, hydroxyC₁₋₆ alkyloxy, C₁₋₆ alkyloxyC₁₋₆ alkyloxy, C₁₋₆ alkyloxycarbonyl, aminoC₁₋₆ alkyloxy, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyloxy, Ar¹, Ar¹ C₁₋₆ alkyl, Ar¹ oxy, Ar¹ C₁₋₆ alkyloxy;

R³ and R⁴ each independently are hydrogen, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxy, Ar¹ oxy, C₁₋₆ alkylthio, di(C₁₋₆ alkyl)amino, trihalomethyl or trihalomethoxy;

R⁵ is hydrogen, halo, C₁₋₆ alkyl, cyano, haloC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, cyanoC₁₋₆

alkyl, aminoC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkylthioC₁₋₆ alkyl, aminocarbonylC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl, Ar¹, Ar¹ C₁₋₆ alkyloxyC₁₋₆ alkyl; or a radical of formula:



wherein

R¹⁰ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, Ar¹, Ar¹ C₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, or a radical of formula --Alk--OR¹³ or --Alk--NR¹⁴R¹⁵;

R¹¹ is hydrogen, C₁₋₆ alkyl, Ar¹ or Ar¹ C₁₋₆ alkyl;

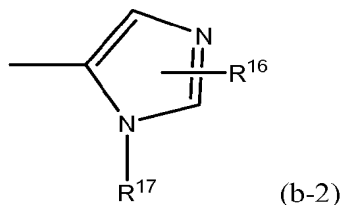
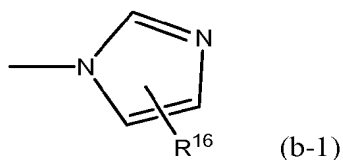
R¹² is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylaminocarbonyl, Ar¹, Ar¹ C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl-C₁₋₆ alkyl, Ar¹ carbonyl, Ar¹ C₁₋₆ alkylcarbonyl, aminocarbonylcarbonyl, C₁₋₆ alkyloxyC₁₋₆ alkylcarbonyl, hydroxy, C₁₋₆ alkyloxy, aminocarbonyl, di(C₁₋₆ alkyl)aminoC₁₋₆ alkylcarbonyl, amino, C₁₋₆ alkylamino, C₁₋₆ alkylcarbonylamino, or a radical of formula --Alk--OR¹³ or --Alk--NR¹⁴R¹⁵; wherein Alk is C₁₋₆ alkanediyl;

R¹³ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, hydroxyC₁₋₆ alkyl, Ar¹ or Ar¹ C₁₋₆ alkyl;

R¹⁴ is hydrogen, C₁₋₆ alkyl, Ar¹ or Ar¹ C₁₋₆ alkyl;

R¹⁵ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, Ar¹ or Ar¹ C₁₋₆ alkyl;

R⁶ is a radical of formula:



wherein

R¹⁶ is hydrogen, halo, Ar¹, C₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkyloxy, C₁₋₆ alkylthio, amino, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylthioC₁₋₆ alkyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl;

R^{17} is hydrogen, C_{1-6} alkyl or $di(C_{1-4}$ alkyl)aminosulfonyl;

R^7 is hydrogen or C_{1-6} alkyl provided that the dotted line does not represent a bond;

R^8 is hydrogen, C_{1-6} alkyl or $Ar^2 CH_2$ or $Het^1 CH_2$;

R^9 is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy or halo; or

R^8 and R^9 taken together to form a bivalent radical of formula

$-CH=CH-$ (c-1)

$-CH_2-CH_2-$ (c-2)

$-CH_2-CH_2-CH_2-$ (c-3)

$-CH_2-O-$ (c-4), or

$-CH_2-CH_2-O-$ (c-5)

Ar^1 is phenyl; or phenyl substituted with 1 or 2 substituents each independently selected from halo, C_{1-6} alkyl, C_{1-6} alkyloxy or trifluoromethyl;

Ar^2 is phenyl; or phenyl substituted with 1 or 2 substituents each independently selected from halo, C_{1-6} alkyl, C_{1-6} alkyloxy or trifluoromethyl; and

Het^1 is pyridinyl; pyridinyl substituted with 1 or 2 substituents each independently selected from halo, C_{1-6} alkyl, C_{1-6} alkyloxy or trifluoromethyl.

132. The method according to claim 131, wherein R^1 and R^2 are each independently selected from hydrogen, halo or C_{1-4} alkyl, R^3 and R^4 are each independently selected from hydrogen, halo or C_{1-4} alkyl, R^5 is hydrogen, hydroxy, halo or a amino; R^6 is a radical of formula (b-1) or (b-2) wherein R^{16} is hydrogen or C_{1-4} alkyl and R^{17} is C_{1-4} alkyl; R^7 is hydrogen or C_{1-4} alkyl in case the dotted line does not represent a bond; R^8 is hydrogen; C_{1-4} alkyl or $Het^1 CH_2$; and R^9 is hydrogen.

133. The method according to claim 131 wherein X is oxygen, R^1 is 3-chloro, R^2 is hydrogen, R^3 is 4-chloro, R^4 is hydrogen, R^5 is hydrogen, C_{1-2} alkyl, halo or amino; R^6 is a radical of formula (b-1) or (b-2) wherein R^{16} is hydrogen and R^{17} is C_{1-2} alkyl; and R^7 is hydrogen or C_{1-2} alkyl in case the dotted line does not represent a bond; R^8 is hydrogen; C_{1-2} alkyl or $Het^1 CH_2$; and R^9 is hydrogen.

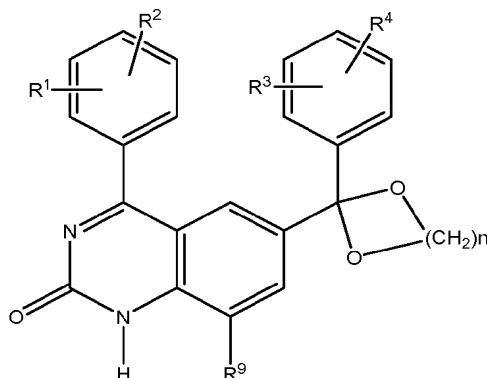
134. The method according to claim 131, wherein the compound is

6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinazolinone;

6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-chlorophenyl)-

3,4-dihydro-1,3-dimethyl-2(1H)-quinazolinone;
or a pharmaceutically acceptable stereoisomer or salt thereof.

135. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject with a lysosomal storage disease a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof, wherein n is 2 or 3; and R¹, R², R³, R⁴, and R⁹ are as defined in claim 49.

136. The method of any one of claims 131-135, wherein the therapeutically effective amount comprises about 10 ng/kg of body weight to about 1000 mg/kg of body weight at a frequency of administration from once a day to once a month.

137. The method of claim 136, further comprising administering to the subject a therapeutically effective amount of one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

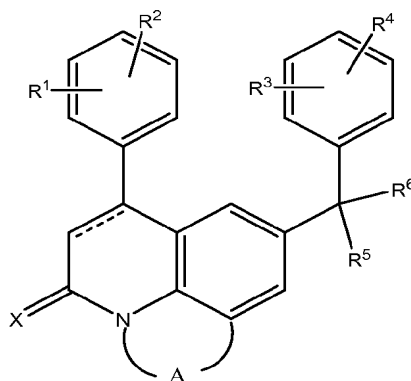
138. An article of manufacture comprising packaging material and a farnesyl transferase inhibitor compound according to any of claims 131-135, wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

139. The article of manufacture of claim 138, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator

protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

140. The article of manufacture of claim 138 further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

141. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject with a lysosomal storage disease a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof, wherein

the dotted line represents an optional bond;

X is oxygen or sulfur;

-A- is a bivalent radical of formula:

-CH=CH- (a-1),

-CH₂-CH₂- (a-2),

-CH₂-CH₂-CH₂- (a-3),

-CH₂-O- (a-4),

- CH₂-CH₂-O- (a-5),
 -CH₂-S- (a-6),
 -CH₂-CH₂-S- (a-7),
 -CH=N- (a-8),
 -N=N- (a-9), or
 -CO-NH- (a-10);

R¹ and R² each independently are hydrogen, hydroxy, halo, cyano, C₁₋₆ alkyl, trihalomethyl, trihalomethoxy, C₂₋₆ alkenyl, C¹⁻⁶ alkyloxy, hydroxy C₁₋₆ alkyloxy, C₁₋₆ alkyloxyC₁₋₆ alkyloxy, C₁₋₆ alkyloxycarbonyl, aminoC₁₋₆ alkyloxy, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyloxy, Ar², Ar² --C₁₋₆ alkyl, Ar² -oxy, Ar² --C₁₋₆ alkyloxy; or

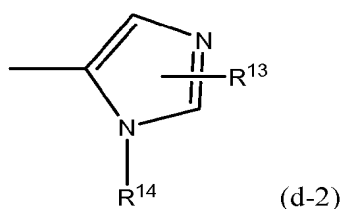
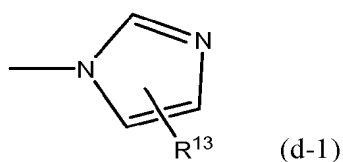
when on adjacent positions R¹ and R² taken together may form a bivalent radical of formula:

- O-CH₂-O- (b-1),
 -O-CH₂-CH₂-O- (b-2),
 -O-CH=CH- (b-3),
 -O-CH₂-CH₂- (b-4),
 -O-CH₂-CH₂-CH₂- (b-5), or
 -CH=CH-CH=CH- (b-6);

R³ and R⁴ each independently are hydrogen, halo, cyano, C₁₋₆alkyl, C₁₋₆alkoxy, Ar³-oxy, C₁₋₆alkylthio, di(C₁₋₆alkyl)amino, trihalomethyl, trihalomethoxy, or when on adjacent positions R³ and R⁴ taken together may form a bivalent radical of formula:

- O-CH₂-O- (c-1),
 -O-CH₂-CH₂-O- (c-2), or
 -CH=CH-CH=CH- (c-3);

R⁵ is a radical of formula:



wherein R¹³ is hydrogen, halo, Ar⁴, C₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆

alkyloxy, C₁₋₆ alkylthio, amino, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl; R¹⁴ is hydrogen, C₁₋₆ alkyl or di(C₁₋₄ alkyl)aminosulfonyl;

R⁶ is hydrogen, hydroxy, halo, C₁₋₆ alkyl, cyano, haloC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, cyanoC₁₋₆ alkyl, aminoC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkylthioC₁₋₆ alkyl, aminocarbonyl-C₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl, Ar⁵, Ar⁵ --C₁₋₆ alkyloxyC₁₋₆ alkyl; or a radical of formula



wherein

R⁷ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, Ar⁶, Ar⁶ --C₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, or a radical of formula --Alk--OR¹⁰ or --Alk--NR¹¹ R¹²;

R⁸ is hydrogen, C₁₋₆ alkyl, Ar⁷ or Ar⁷ --C₁₋₆ alkyl;

R⁹ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylaminocarbonyl, Ar⁸, Ar⁸ -C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl-C₁₋₆ alkyl, Ar⁸ -carbonyl, Ar⁸ --C₁₋₆ alkylcarbonyl, aminocarbonylcarbonyl, C₁₋₆ alkyloxyC₁₋₆ alkylcarbonyl, hydroxy, C₁₋₆ alkyloxy, aminocarbonyl, di(C₁₋₆ alkyl)aminoC₁₋₆ alkylcarbonyl, amino, C₁₋₆ alkylamino, C₁₋₆ alkylcarbonylamino, or a radical or formula --Alk--OR¹⁰ or --Alk--NR¹¹ R¹²;

wherein Alk is C₁₋₆ alkanediyl;

R¹⁰ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, hydroxyC₁₋₆ alkyl, Ar⁹ or Ar⁹ --C₁₋₆ alkyl;

R¹¹ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, Ar¹⁰ or Ar¹⁰ --C₁₋₆ alkyl;

R¹² is hydrogen, C₁₋₆ alkyl, Ar¹¹ or Ar¹¹ -C₁₋₆ alkyl; and

Ar¹ to Ar¹¹ are each independently selected from phenyl; or phenyl substituted with halo, C₁₋₆ alkyl, C₁₋₆ alkyloxy or trifluoromethyl.

142. The method according to claim 141, wherein the dotted line represents an optional bond;

X is O or S;

R¹ and R² are each independently selected from hydrogen, halo, C₁₋₆ alkyl, C₁₋₆ alkyloxy, trihalomethyl or trihalomethoxy;

R³ and R⁴ are each independently selected from hydrogen, halo, C₁₋₆ alkyl, C₁₋₆ alkyloxy, trihalomethyl or trihalomethoxy;

R^5 a radical of formula (d-1) wherein R^{13} is hydrogen or R^5 is a radical of formula (d-2) wherein R^{13} is hydrogen or C_{1-6} alkyl and R^{14} is hydrogen or C_{1-6} alkyl;

R^6 is hydrogen, hydroxy, halo C_{1-6} alkyl, hydroxy C_{1-6} alkyl, cyano C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, or a radical of formula $-NR^8R^9$ wherein R^8 is hydrogen or C_{1-6} alkyl and R^9 is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy or C_{1-6} alkyloxy C_{1-6} alkylcarbonyl.

143. The method according to claim 141, wherein X is oxygen; the dotted line represents a bond; R^1 is 3-halo; R^2 is hydrogen; R^3 is 4-halo; R^4 is hydrogen; R^5 a radical of formula (d-1) wherein R^{13} is hydrogen or R^5 is a radical of formula (d-2) wherein R^{13} is hydrogen and R^{14} is C_{1-4} alkyl; R^6 is hydrogen, halo, hydroxy or amino; and -A- is (a-1), (a-2) or (a-3).

144. The method according to claim 141 wherein the compound is:

7-(3-chlorophenyl)-9-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]-2,3-dihydro-1H,5H-benzo[*ij*]quinolizin-5-one;

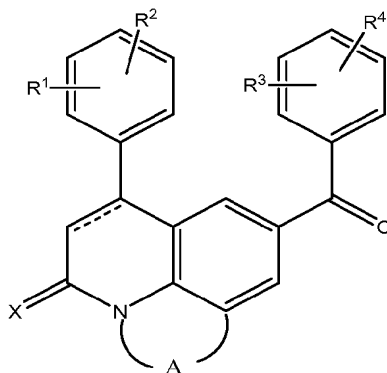
7-(3-chlorophenyl)-9-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]-1,2-dihydro-4H-pyrrolo[3,2-*ij*]quinoline-4-one;

8-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-6-(3-chlorophenyl)-1,2-dihydro-4H-pyrrolo[3,2-*ij*]quinolin-4-one;

8-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-6-(3-chlorophenyl)-2,3-dihydro-1H,5H-benzo[*ij*]quinolizin-5-one; or

a pharmaceutically acceptable stereoisomer, isomer, or salt thereof.

145. The method of claim 141 wherein the farnesyl transferase inhibitor compound has the structure:



or a pharmaceutically acceptable stereoisomer, isomer, or salt thereof, wherein the dotted line

represents an optional bond; and wherein X, -A-, R¹, R², R³, and R⁴ are as defined in claim 141.

146. The method of any one of claims 141-145, wherein the therapeutically effective amount comprises about 10ng/kg of body weight to about 1000mg/kg of body weight at a frequency of administration from once a day to once a month.

147. The method of claim 146, further comprising administering to the subject an amount of one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

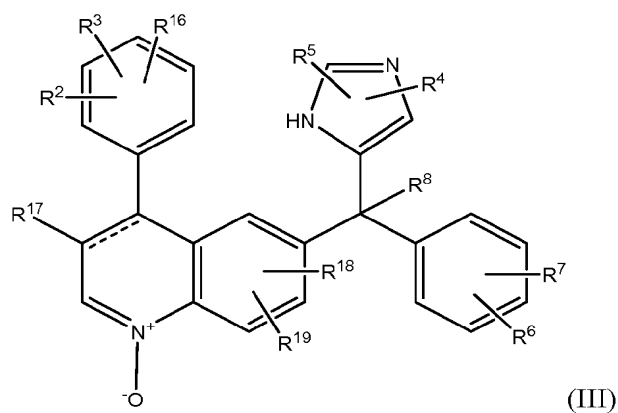
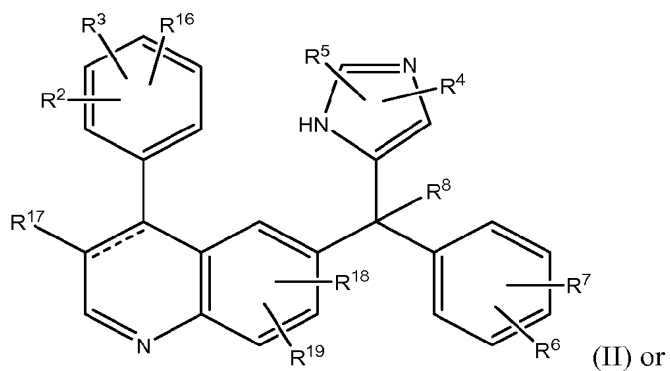
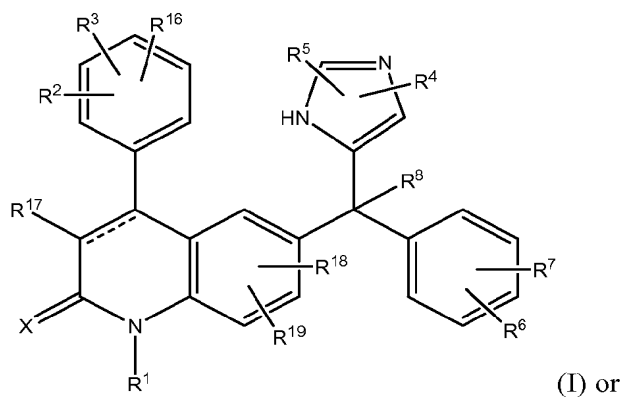
148. An article of manufacture comprising packaging material and a farnesyl transferase inhibitor compound according to any one of claims 141-145, wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

149. The article of manufacture of claim 148, wherein the neurodegenerative disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucopolisulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanizaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknotodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

150. The article of manufacture of claim 148, further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

151. A method of treating a subject with a lysosomal storage disease, the method

comprising administering to a subject with a lysosomal storage disease a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable derivative, analog, stereoisomer, isomer, solvate, or salt thereof,

wherein

the dotted line represents an optional bond;

X is oxygen or sulfur;

R¹ is hydrogen, C₁₋₁₂ alkyl, Ar¹, Ar² C₁₋₆ alkyl, quinolinylC₁₋₆ alkyl, pyridylC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, mono- or di (C₁₋₆ alkyl) aminoC₁₋₆ alkyl, aminoC₁₋

$_6$ alkyl, or a radical of formula $-\text{Alk}^1-\text{C}(=\text{O})-\text{R}^9$, $-\text{Alk}^1-\text{S}(\text{O})-\text{R}^9$ or $-\text{Alk}^1-\text{S}(\text{O})_2-\text{R}^9$,
wherein

Alk^1 is C_{1-6} alkanediyl,

R^9 is hydroxy, C_{1-6} alkyl, C_{1-6} alkyloxy, amino, C_{1-8} alkylamino or C_{1-8} alkylamino substituted with C_{1-6} alkyloxycarbonyl;

R^2 , R^3 and R^{16} each independently are hydrogen, hydroxy, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxy, hydroxy C_{1-6} alkyloxy, C_{1-6} alkyloxy C_{1-6} alkyloxy, amino C_{1-6} alkyloxy, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyloxy, Ar^1 , Ar^2 C_{1-6} alkyl, Ar^2 oxy, Ar^2 C_{1-6} alkyloxy, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, trihalomethyl, trihalomethoxy, C_{2-6} alkenyl, 4,4-dimethyloxazolyl; or

when on adjacent positions R^2 and R^3 taken together may form a bivalent radical of formula

$-\text{O}-\text{CH}_2-\text{O}-$ (a-1),

$-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-$ (a-2)

$-\text{O}-\text{CH}=\text{CH}-$ (a-3)

$-\text{O}-\text{CH}_2-\text{CH}_2-$ (a-4)

$-\text{O}-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ (a-5), or

$-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ (a-6);

R^4 and R^5 each independently are hydrogen, halo, Ar^1 , C_{1-6} alkyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, C_{1-6} alkyloxy, C_{1-6} alkylthio, amino, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylS(O) C_{1-6} alkyl or C_{1-6} alkylS(O) $_2$ C_{1-6} alkyl;

R^6 and R^7 each independently are hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} alkyloxy, Ar^2 oxy, trihalomethyl, C_{1-6} alkylthio, di (C_{1-6} alkyl) amino, or

when on adjacent positions R^6 and R^7 taken together may form a bivalent radical of formula

$-\text{O}-\text{CH}_2-\text{O}-$ (c-1), or

$-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ (c-2);

R^8 is hydrogen, C_{1-6} alkyl, cyano, hydroxycarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, cyanoc C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6} alkyl, carboxy C_{1-6} alkyl, hydroxy C_{1-6} alkyl, amino C_{1-6} alkyl, mono- or di (C_{1-6} alkyl)-amino C_{1-6} alkyl, imidazolyl, halo C_{1-6} alkyl, C_{1-6} alkyloxy- C_{1-6} alkyl, aminocarbonyl C_{1-6} alkyl, or a radical of formula

$-\text{O}-\text{R}^{10}$ (b-1),

$-\text{S}-\text{R}^{10}$ (b-2),

$-\text{N}-\text{R}^{11} \text{R}^{12}$ (b-3),

wherein

R^{10} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 , Ar^2 C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl C_{1-6}

alkyl, a radical or formula $-\text{Alk}^2 -\text{OR}^{13}$ or $-\text{Alk}^2 -\text{NR}^{14} \text{R}^{15}$;

R^{11} is hydrogen, C_{1-12} alkyl, Ar^1 or $\text{Ar}^2 \text{C}_{1-6}$ alkyl;

R^{12} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6}

alkylaminocarbonyl, Ar^1 , $\text{Ar}^2 \text{C}_{1-6}$ alkyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, a natural amino acid,

Ar^1 carbonyl, $\text{Ar}^2 \text{C}_{1-6}$ alkylcarbonyl, aminocarbonylcarbonyl, C_{1-6} alkyloxy C_{1-6} alkyl-

carbonyl, hydroxy, C_{1-6} alkyloxy, aminocarbonyl, di(C_{1-6} alkyl)amino C_{1-6} alkylcarbonyl,

amino, C_{1-6} alkylamino, C_{1-6} alkylcarbonylamino, or a radical of formula $-\text{Alk}^2 -\text{OR}^{13}$ or -

$\text{Alk}^2 -\text{NR}^{14} \text{R}^{15}$;

wherein

Alk^2 is C_{1-6} alkanediyl;

R^{13} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, hydroxy C_{1-6} alkyl, Ar^1 or $\text{Ar}^2 \text{C}_{1-6}$ alkyl;

R^{14} is hydrogen, C_{1-6} alkyl, Ar^1 or $\text{Ar}^2 \text{C}_{1-6}$ alkyl;

R^{15} is hydrogen, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, Ar^1 or $\text{Ar}^2 \text{C}_{1-6}$ alkyl;

R^{17} is hydrogen, halo, cyano, C_{1-6} alkyl, C_{1-6} -alkyloxycarbonyl, Ar^1 ;

R^{18} is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy or halo;

R^{19} is hydrogen or C_{1-6} alkyl;

Ar^1 is phenyl or phenyl substituted with C_{1-6} alkyl, hydroxy, amino, C_{1-6} alkyloxy or halo;

and

Ar^2 is phenyl or phenyl substituted with C_{1-6} alkyl, hydroxy, amino, C_{1-6} alkyloxy or halo.

152. The method of claim 151 wherein the farnesyl transferase inhibitor is a compound of formula (I) and wherein X is oxygen.

153. The method of claim 151 wherein the farnesyl transferase inhibitor is a compound of formula (I) and wherein the dotted line represents a bond.

154. The method of claim 151 wherein the farnesyl protein transferase inhibitor is a compound of formula (I) and wherein R^1 is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl or mono- or di (C_{1-6} alkyl)amino C_{1-6} alkyl.

155. The method of claim 151 wherein the farnesyl protein transferase inhibitor is a compound of formula (I) and wherein R^3 is hydrogen and R^2 is halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkyloxy, trihalomethoxy or hydroxy C_{1-6} alkyloxy.

156. The method of claim 151 wherein the farnesyl protein transferase inhibitor is a compound of formula (I) and wherein R^8 is hydrogen, hydroxy, haloC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, cyanoC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, imidazolyl, or a radical of formula --NR¹¹R¹² wherein R¹¹ is hydrogen or C₁₋₁₂ alkyl and R¹² is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkyloxy, C₁₋₆ alkyloxyC₁₋₆ alkylcarbonyl, hydroxy, or a radical of formula -Alk²-OR¹³ wherein R¹³ is hydrogen or C₁₋₆ alkyl.

157. The method of claim 151 wherein the compound is 4-(3-chlorophenyl)-6-[(4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl]-1-methyl-2(1H)-quinolinone, 6-[amino(4-chlorophenyl)-1-methyl-1H-imidazol-5-ylmethyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone; 6-[(4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-ethoxy-phenyl)-1-methyl-2(1H)-quinolinone; 6-[(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-ethoxyphenyl)-1-methyl-2(1H)-quinolinone monohydrochloride.monohydrate; 6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-ethoxyphenyl)-1-methyl-2(1H)-quinolinone, and 6-amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-1-methyl-4-(3-propylphenyl)-2(1H)-quinolinone; or a pharmaceutically acceptable isomer, stereoisomer, solvate, or salt thereof.

158. The method of claim 151 wherein the compound is (+)-6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-chloro-phenyl)-1-methyl-2(1H)-quinolinone; or a pharmaceutically acceptable acid addition salt thereof.

159. The method of any one of claims 151-158 wherein the effective amount comprises about 10ng/kg of body weight to about 1000mg/kg of body weight at a frequency of administration from once a day to once a month.

160. The method of claim 151 or 159, further comprising administering to the subject an amount of one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

161. The method of claim 160, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

162. An article of manufacture comprising packaging material and a farnesyl transferase

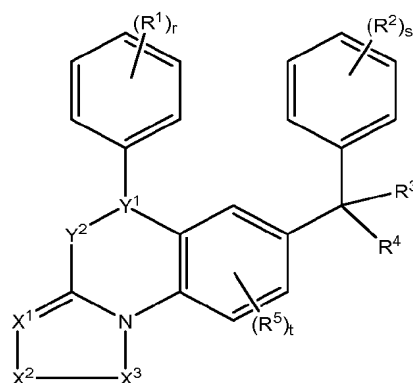
inhibitor compound according to any one of claims 151-158, wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

163. The article of manufacture of claim 162, wherein the neurodegenerative disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

164. The article of manufacture of claim 162 further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

165. The article of manufacture of claim 164, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

166. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof, in a therapeutically effective amount,
wherein

$=X^1-X^2-X^3-$ is a trivalent radical of formula

$=N-CR^6=CR^7-$ (x-1),

$=N-N=CR^6-$ (x-2),

$=N-NH-C(=O)-$ (x-3),

$=N-N=N-$ (x-4),

$=N-CR^6=N-$ (x-5),

$=CR^6-CR^7=CR^8-$ (x-6),

$=CR^6-N=CR^7-$ (x-7),

$=CR^6-NH-C(=O)-$ (x-8), or

$=CR^6-N=N-$ (x-9);

wherein each R^6 , R^7 and R^8 are independently hydrogen, C_{1-4} alkyl, hydroxy, C_{1-4} alkyloxy, aryloxy, C_{1-4} alkyloxycarbonyl, hydroxy C_{1-6} alkyl, C_{1-4} alkyloxy C_{1-4} alkyl, mono- or di(C_{1-6} alkyl)amino C_{1-4} alkyl, cyano, amino, thio, C_{1-4} alkylthio, arylthio or aryl;

$>Y^1-Y^2$ is a trivalent radical of formula

$>CH-CHR^9-$ (y-1),

$>C=N-$ (y-2),

$>CH-NR^9-$ (y-3), or

$>C=CR^9-$ (y-4);

wherein each R^9 independently is hydrogen, halo, halocarbonyl, aminocarbonyl, hydroxy C_{1-4} alkyl, cyano, carboxyl, C_{1-4} alkyl, C_{1-4} alkyloxy, C_{1-4} alkyloxy C_{1-4} alkyl, C_{1-4} alkyloxycarbonyl, mono- or di(C_{1-6} alkyl)amino, mono- or di(C_{1-4} alkyl)amino C_{1-4} alkyl, or aryl;

r and s are each independently 0, 1, 2, 3, 4 or 5;

t is 0, 1, 2 or 3;

each R¹ and R² are independently hydroxy, halo, cyano, C₁₋₆ alkyl, trihalomethyl, trihalomethoxy, C₂₋₆ alkenyl, C₁₋₆ alkyloxy, hydroxyC₁₋₆ alkyloxy, C₁₋₆ alkylthio, C₁₋₆ alkyloxyC₁₋₆ alkyloxy, C₁₋₆ alkyloxycarbonyl, aminoC₁₋₆ alkyloxy, mono- or di(C₁₋₆ alkyl)amino, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyloxy, aryl, arylC₁₋₆ alkyl, aryloxy or arylC₁₋₆ alkyloxy, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, aminocarbonyl, aminoC₁₋₆ alkyl, mono- or di(C₁₋₆ alkyl)aminocarbonyl, or mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl; or

two R¹ or R² substituents adjacent to one another on the phenyl ring independently form together a bivalent radical of formula

-O-CH₂-O- (a-1),

-O-CH₂-CH₂-O- (a-2),

-O=CH=CH- (a-3),

-O-CH₂-CH₂- (a-4),

-O-CH₂-CH₂-CH₂- (a-5), or

-CH=CH-CH=CH- (a-6);

R³ is hydrogen, halo, C₁₋₆ alkyl, cyano, haloC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, cyanoC₁₋₆ alkyl, aminoC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkylthioC₁₋₆ alkyl, aminocarbonyl, C₁₋₆ alkyl, hydroxycarbonyl, hydroxycarbonylC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonyl, aryl, arylC₁₋₆ alkyloxyC₁₋₆ alkyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl; or a radical of formula

-O-R¹⁰ (b-1),

-S-R¹⁰ (b-2), or

-NR¹¹ R¹² (b-3),

wherein R¹⁰ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, aryl, arylC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonyl C₁₋₆ alkyl, or a radical of formula -Alk--OR¹³ or -Alk--NR¹⁴ R¹⁵ ;

R¹¹ is hydrogen, C₁₋₆ alkyl, aryl or arylC₁₋₆ alkyl;

R¹² is hydrogen, C₁₋₆ alkyl, aryl, hydroxy, amino, C₁₋₆ alkyloxy, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, arylC₁₋₆ alkyl, C₁₋₆ alkylcarbonylamino, mono- or di(C₁₋₆ alkyl)amino, C₁₋₆ alkylcarbonyl, aminocarbonyl, arylcarbonyl, haloC₁₋₆ alkylcarbonyl, arylC₁₋₆ alkylcarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkyloxyC₁₋₆ alkylcarbonyl, mono- or di(C₁₋₆ alkyl)aminocarbonyl wherein the alkyl moiety may optionally be substituted by one or more substituents independently selected from aryl or C₁₋₃ alkyloxycarbonyl, aminocarbonylcarbonyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkylcarbonyl, or a radical of formula -Alk--OR¹³ or -Alk--NR¹⁴ R¹⁵ ;

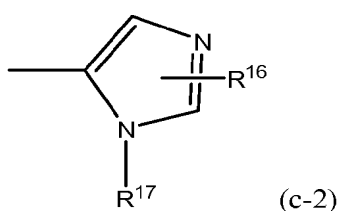
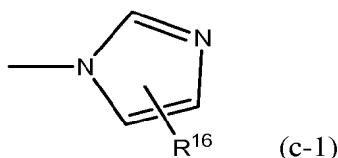
wherein Alk is C₁₋₆ alkanediyl;

R¹³ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, hydroxyC₁₋₆ alkyl, aryl or arylC₁₋₆ alkyl;

R¹⁴ is hydrogen, C₁₋₆ alkyl, aryl or arylC₁₋₆ alkyl;

R¹⁵ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, aryl or arylC₁₋₆ alkyl;

R⁴ is a radical of formula



wherein R¹⁶ is hydrogen, halo, aryl, C₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkyloxy, C₁₋₆ alkylthio, amino, mono- or di(C₁₋₄ alkyl)amino, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylthioC₁₋₆ alkyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl;

R¹⁷ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, arylC₁₋₆ alkyl, trifluoromethyl or di(C₁₋₄ alkyl)aminosulfonyl;

R⁵ is C₁₋₆ alkyl, C₁₋₆ alkyloxy or halo; aryl is phenyl, naphthalenyl or phenyl substituted with one or more substituents each independently selected from halo, C₁₋₆ alkyl, C₁₋₆ alkyloxy or trifluoromethyl; with the proviso that that when R¹⁶ is bound to one of the nitrogen atoms in the imidazole ring of formula (c-1) or (c-2), R¹⁶ is hydrogen, aryl, C₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl.

167. The method according to claim 166, wherein each R¹ and R² are independently hydroxy, halo, cyano, C₁₋₆ alkyl, trihalomethyl, trihalomethoxy, C₂₋₆ alkenyl, C₁₋₆ alkyloxy, hydroxyC₁₋₆ alkyloxy, C₁₋₆ alkylthio, C₁₋₆ alkyloxyC₁₋₆ alkyloxy, C₁₋₆ alkyloxycarbonyl, aminoC₁₋₆ alkyloxy, mono- or di(C₁₋₆ alkyl)amino, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyloxy, aryl, arylC₁₋₆ alkyl, aryloxy or arylC₁₋₆ alkyloxy, hydroxycarbonyl, or C₁₋₆ alkyloxycarbonyl; or

two R¹ or R² substituents adjacent to one another on the phenyl ring independently form together a bivalent radical of formula

-O-CH₂-O- (a-1),

-O-CH₂-CH₂-O- (a-2),

-O=CH=CH- (a-3),

-O-CH₂-CH₂- (a-4),

-O-CH₂-CH₂-CH₂- (a-5), or

-CH=CH-CH=CH- (a-6);

R¹⁷ is hydrogen, C₁₋₆ alkyl, trifluoromethyl or di(C₁₋₆ alkyl)aminosulfonyl;

with the proviso that that when R¹⁶ is bound to one of the nitrogen atoms in the imidazole ring of formula (c-1), R¹⁶ is hydrogen, aryl, C₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl.

168. The method according to claim 166, wherein =X¹--X²--X³ is a trivalent radical of formula (x-1), (x-2), (x-3), (x-4) or (x-9) wherein each R⁶ independently is hydrogen, C₁₋₄ alkyl, C₁₋₆ alkyloxycarbonyl, amino or aryl and R⁷ is hydrogen; >Y¹--Y²-- is a trivalent radical of formula (y-1), (y-2), (y-3), or (y-4) wherein each R⁹ independently is hydrogen, halo, carboxyl, C₁₋₄ alkyl or C₁₋₄ alkyloxycarbonyl; r is 0, 1 or 2; s is 0 or 1; t is 0; R¹ is halo, C₁₋₆ alkyl or two R¹ substituents ortho to one another on the phenyl ring independently form together a bivalent radical of formula (a-1); R² is halo; R³ is halo or a radical of formula (b-1) or (b-3) wherein R¹⁰ is hydrogen or a radical of formula -Alk-OR¹³, R¹¹ is hydrogen, R¹² is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, hydroxy, C₁₋₆ alkyloxy or mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkylcarbonyl, Alk is C₁₋₆ alkanediyl and R¹³ is hydrogen; R⁴ is a radical of formula (c-1) or (c-2) wherein R¹⁶ is hydrogen, halo or mono- or di(C₁₋₄ alkyl)amino; R¹⁷ is hydrogen or C₁₋₆ alkyl; aryl is phenyl.

169. The method according to claim 166, wherein =X¹--X²--X³ is a trivalent radical of formula (x-1), >Y¹--Y² is a trivalent radical of formula (y-4), r is 0 or 1, s is 1, t is 0, R³ is 3-chloro, R² is 4-chloro or 4-fluoro, R³ is hydrogen or a radical of formula (b-1) or (b-3), R⁴ is a radical of formula (c-1) or (c-2), R⁶ is hydrogen, R⁷ is hydrogen, R⁹ is hydrogen, R¹⁰ is hydrogen, R¹¹ is hydrogen and R¹² is hydrogen.

170. The method according to claim 166, wherein =X¹--X²--X³ is a trivalent radical of

formula (x-2) or (x-3), $>Y^1 - Y^2$ is a trivalent radical of formula (y-2), (y-3) or (y-4), r and s are 1, t is 0, R^1 is 3-chloro or 3-methyl, R^2 is 4-chloro, R^3 is a radical of formula (b-1) or (b-3), R^4 is a radical of formula (c-2), R^6 is C_{1-4} alkyl, R^9 is hydrogen, R^{10} and R^{11} are hydrogen and R^{12} is hydrogen or hydroxy.

171. The method according to claim 166, wherein the farnesyl transferase inhibiting compound is selected from:

7-[(4-fluorophenyl)(1H-imidazol-1-yl)methyl]-5-phenylimidazo [1,2-a]quinoline; α -(4-chlorophenyl)-.alpha.-(1-methyl-1H-imidazol-5-yl)-5-phenylimidazo[1,2-a]quinoline-7-methanol; 5-(3-chlorophenyl)-.alpha.-(4-chlorophenyl)-.alpha.-(1-methyl-1H-imidazol-5-yl)-imidazo[1,2-a]quinoline-7-methanol; 5-(3-chlorophenyl)- α -(4-chlorophenyl)-.alpha.-(1-methyl-1H-imidazol-5-yl)imidazo[1,2-a]quinoline-7-methanamine; 5-(3-chlorophenyl)- α -(4-chlorophenyl)- α -(1-methyl-1H-imidazol-5-yl)tetrazolo[1,5-a]quinoline-7-methanamine; 5-(3-chlorophenyl)- α -(4-chlorophenyl)-1-methyl- α -(1-methyl-1H-imidazol-5-yl)-1,2,4-triazolo[4,3-a]quinoline-7-methanol; 5-(3-chlorophenyl)- α -(4-chlorophenyl)- α -(1-methyl-1H-imidazol-5-yl)tetrazolo[1,5-a]quinoline-7-methanamine; 5-(3-chlorophenyl)- α -(4-chlorophenyl)- α -(1-methyl-1H-imidazol-5-yl)tetrazolo[1,5-a]quinazoline-7-methanol; 5-(3-chlorophenyl)- α -(4-chlorophenyl)-4,5-dihydro- α -(1-methyl-1H-imidazol-5-yl)tetrazolo[1,5-a]quinazoline-7-methanol; 5-(3-chlorophenyl)- α -(4-chlorophenyl)- α -(1-methyl-1H-imidazol-5-yl)tetrazolo[1,5-a]quinazoline-7-methanamine; 5-(3-chlorophenyl)- α -(4-chlorophenyl)-N-hydroxy- α -(1-methyl-1H-imidazol-5-yl)tetrahydro[1,5-a]quinoline-7-methanamine; α -(4-chlorophenyl)- α -(1-methyl-1H-imidazol-5-yl)-5-(3-methylphenyl)tetrazolo[1,5-a]quinoline-7-methanamine; a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof.

172. The method of any of claims 166-171, wherein the effective amount comprises about 10ng/kg of body weight to about 1000mg/kg of body weight at a frequency of administration from once a day to once a month.

173. The method of claim 166, further comprising administering to the subject an amount of one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

174. The method of claim 173, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

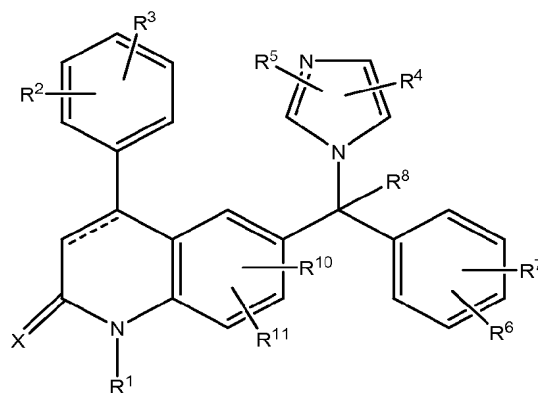
175. An article of manufacture comprising packaging material and a farnesyl transferase inhibitor compound according to any of claims 166-171, wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

176. The article of manufacture of claim 175, wherein the lysosomal storage disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

177. The article of manufacture of claim 175, further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

178. The article of manufacture of claim 177, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

179. A method of treating a subject with a lysosomal storage disease, the method comprising, administering to a subject with a lysosomal storage disease a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof, in a therapeutically effective amount,

wherein

the dotted line represents an optional bond;

X is oxygen or sulfur;

R¹ is hydrogen, C₁₋₁₂ alkyl, Ar¹, Ar² C₁₋₆ alkyl, quinolinylC₁₋₆ alkyl, pyridylC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl, aminoC₁₋₆ alkyl, or a radical of formula -Alk¹-C(=O)-R⁹, -Alk¹-S(O)-R⁹ or -Alk¹-S(O)₂-R⁹, wherein Alk¹ is C₁₋₆ alkanediyl,

R⁹ is hydroxy, C₁₋₆ alkyl, C₁₋₆ alkyloxy, amino, C₁₋₈ alkylamino or C₁₋₈ alkylamino substituted with C₁₋₆ alkyloxycarbonyl;

R² and R³ each independently are hydrogen, hydroxy, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxy, hydroxyC₁₋₆ alkyloxy, C₁₋₆ alkyloxyC₁₋₆ alkyloxy, aminoC₁₋₆ alkyloxy, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyloxy, Ar¹, Ar² C₁₋₆ alkyl, Ar² oxy, Ar² C₁₋₆ alkyloxy, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, trihalomethyl, trihalomethoxy, C₂₋₆ alkenyl; or

when on adjacent positions R² and R³ taken together may form a bivalent radical of formula

-O-CH₂-O- (a-1),

-O-CH₂-CH₂-O- (a-2),

-O-CH=CH- (a-3),

-O-CH₂-CH₂- (a-4),

-O-CH₂-CH₂-CH₂- (a-5), or

-CH=CH-CH=CH- (a-6);

R⁴ and R⁵ each independently are hydrogen, Ar¹, C₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkyloxy, C₁₋₆ alkylthio, amino, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylS(O)C₁₋₆ alkyl or C₁₋₆ alkylS(O)₂ C₁₋₆ alkyl;

R⁶ and R⁷ each independently are hydrogen, halo, cyano, C₁₋₆ alkyl, C₁₋₆ alkyloxy or Ar² oxy;
 R⁸ is hydrogen, C₁₋₆ alkyl, cyano, hydroxycarbonyl, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkylcarbonylC₁₋₆ alkyl, cyanoC₁₋₆ alkyl, C₁₋₆ alkyloxycarbonylC₁₋₆ alkyl, hydroxycarbonylC₁₋₆ alkyl, hydroxyC₁₋₆ alkyl, aminoC₁₋₆ alkyl, mono- or di(C₁₋₆ alkyl)aminoC₁₋₆ alkyl, haloC₁₋₆ alkyl, C₁₋₆ alkyloxyC₁₋₆ alkyl, aminocarbonylC₁₋₆ alkyl, Ar¹, Ar² C₁₋₆ alkyloxyC₁₋₆ alkyl, C₁₋₆ alkylthioC₁₋₆ alkyl;
 R¹⁰ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkyloxy or halo;
 R¹¹ is hydrogen or C₁₋₆ alkyl;
 Ar¹ is phenyl or phenyl substituted with C₁₋₆ alkyl, hydroxy, amino, C₁₋₆ alkyloxy or halo;
 and
 Ar² is phenyl or phenyl substituted with C₁₋₆ alkyl, hydroxy, amino, C₁₋₆ alkyloxy or halo.

180. The method of claim 179, wherein X is oxygen.

181. The method of claim 179, wherein R¹ is hydrogen, C₁₋₆ alkyl or C₁₋₆ alkyloxyC₁₋₆ alkyl.

182. The method of claim 179, wherein R⁶ is hydrogen and R⁷ is halo.

183. The method of claim 179, wherein R⁸ is hydrogen, C₁₋₆ alkyl or hydroxy-C₁₋₆ alkyl.

184. The method of claim 179, wherein the compound is

4-(3-chlorophenyl)-6-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]-1-methyl-2(1H)-quinolinone;

4-(3-chlorophenyl)-6-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]-2(1H)-quinolinone;
 6-[1-(4-chlorophenyl)-2-hydroxy-1-(1H-imidazol-1-yl)ethyl]-1-methyl-4-phenyl-2(1H)-quinolinone;

4-(3-chlorophenyl)-6-[1-(4-chlorophenyl)-1-(1H-imidazol-1-yl)ethyl]-1-methyl-2(1H)-quinolinone;

4-(3-chlorophenyl)-6-[1-(4-chlorophenyl)-1-(5-methyl-1H-imidazol-1-yl)ethyl]-1-methyl-2(1H)-quinolinone;

4-(3-chlorophenyl)-6-[1-(4-chlorophenyl)-2-hydroxy-1-(1H-imidazol-1-yl)ethyl]-1-methyl-2(1H)-quinolinone;

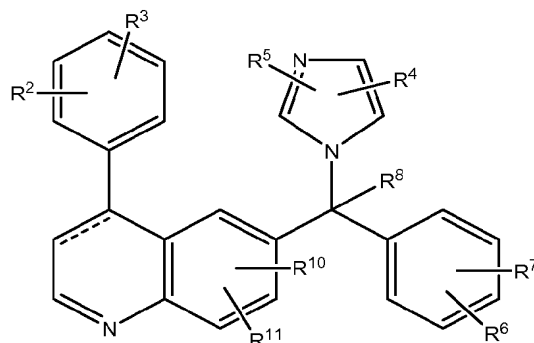
4-(3-chlorophenyl)-6-[(4-chlorophenyl)(1H-imidazol-1-yl)methyl]-1-(2-

methoxyethyl)-2(1H)-quinolinone ethanedioate (2:3) monohydrate;

6-[(4-chlorophenyl)(1H-imidazol-1-yl)methyl]-4-(1,3-benzodioxol-5-yl)-1-methyl-2(1H)-quinolinone ethanedioate (1:1);

or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof.

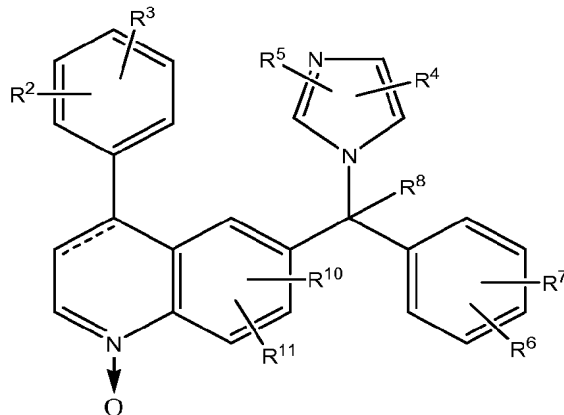
185. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject with a lysosomal storage disease a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable, stereoisomer, isomer, solvate, or salt thereof, in a therapeutically effective amount,

wherein R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_{10} and R_{11} are as defined in claim 4.

186. A method of treating a subject with a lysosomal storage disease, the method comprising, administering to a subject with a lysosomal storage disease a farnesyl transferase inhibitor of formula:



or a pharmaceutically acceptable stereoisomer, isomer, solvate, or salt thereof, in a therapeutically effective amount,

wherein R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₁₀ and R₁₁ are as defined in claim 4.

187. The method of any one of claims 179-186 wherein the effective amount comprises about 10ng/kg of body weight to about 1000mg/kg of body weight at a frequency of administration from once a day to once a month.

188. The method of claim 187, further comprising administering to the subject an amount of one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

189. The method of claim 188, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

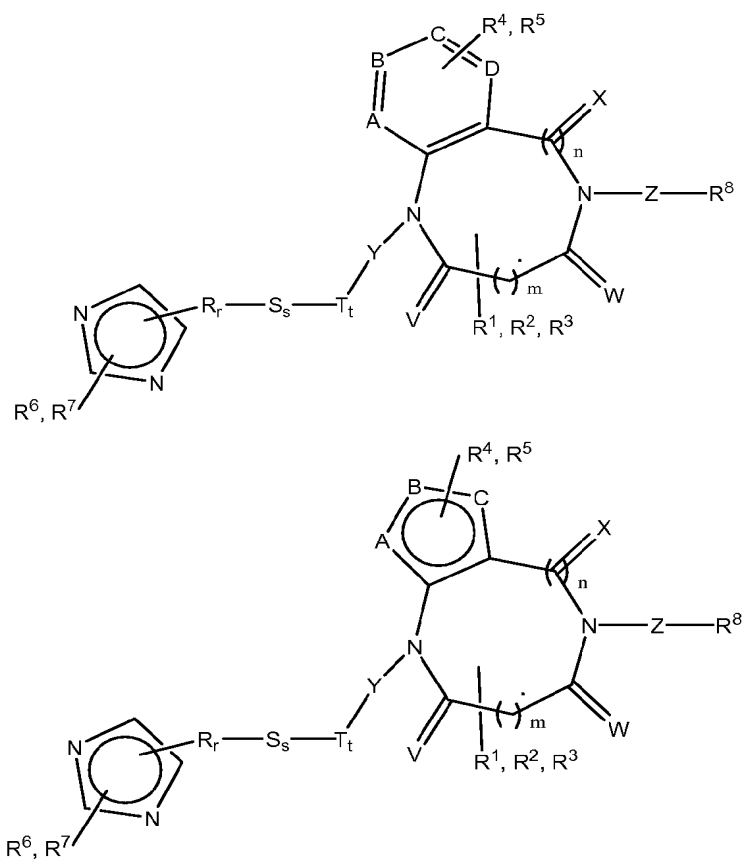
190. An article of manufacture comprising packaging material and a farnesyl transferase inhibitor compound according to any one of claims 179-186, wherein the article of manufacture further comprises a label or package insert indicating that the farnesyl transferase inhibitor compound can be administered to a subject for treating a lysosomal storage disease.

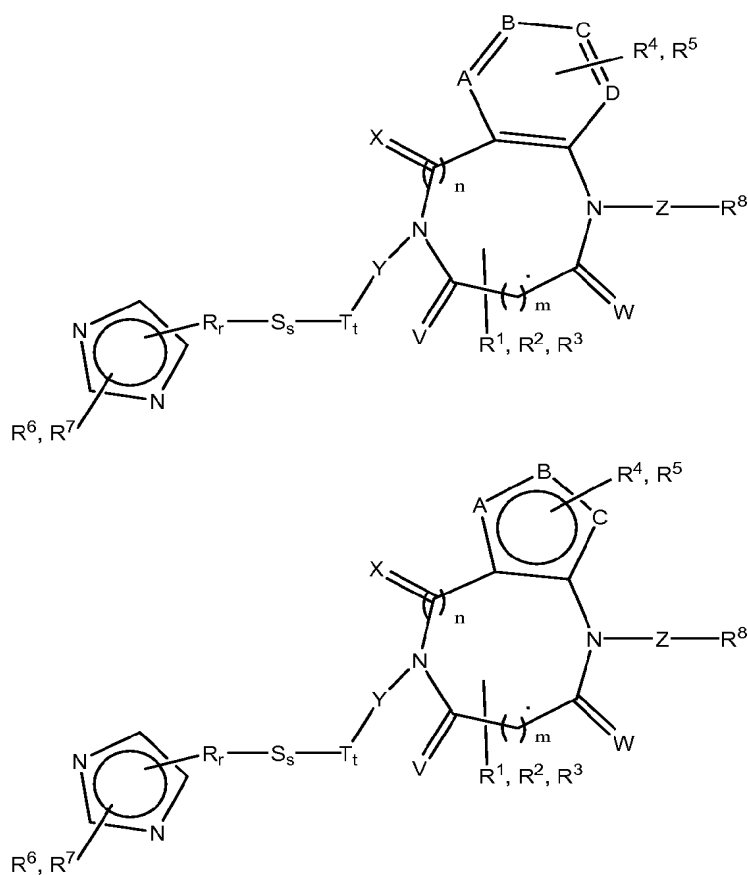
191. The article of manufacture of claim 190, wherein the neurodegenerative disease is selected from the group consisting of glycogen storage disease type II, mucopolysaccharidoses, mucopolipidosis II, mucopolipidosis III, mucosulfatidosis, GM2 activator protein deficiency variant AB, Danon disease, Salla disease, Tay-Sachs disease, Sandhoff disease, Schindler disease, Kanzaki disease, alpha-mannosidosis, beta-mannosidosis, fucosidosis, sialidosis, aspartylglucosaminuria, carbohydrate-deficient glycoprotein syndrome, Wolman disease, Farber disease, Niemann-Pick disease types A, B, and C, Gaucher disease, Krabbe disease, Fabry disease, multiple sulfatase deficiency, GM₁ gangliosidosis, GM₂ gangliosidosis, GM₃ gangliosidosis, galactosialidosis, cystinosis, sialic acid storage disease, pyknodysostosis, metachromatic leukodystrophy, galactosialidosis, neuronal ceroid lipofuscinosis (types 1-9), lactosylceramidosis, Pompe disease, and cobalamin deficiency type F.

192. The article of manufacture of claim 191, further comprising one or more non-farnesyl transferase inhibitor compounds effective to treat a lysosomal storage disease.

193. The article of manufacture of claim 192, wherein the non-farnesyl transferase inhibitor compound comprises enzyme replacement therapy.

194. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject with a lysosomal storage disease a farnesyl transferase inhibitor compound of the formula:





or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

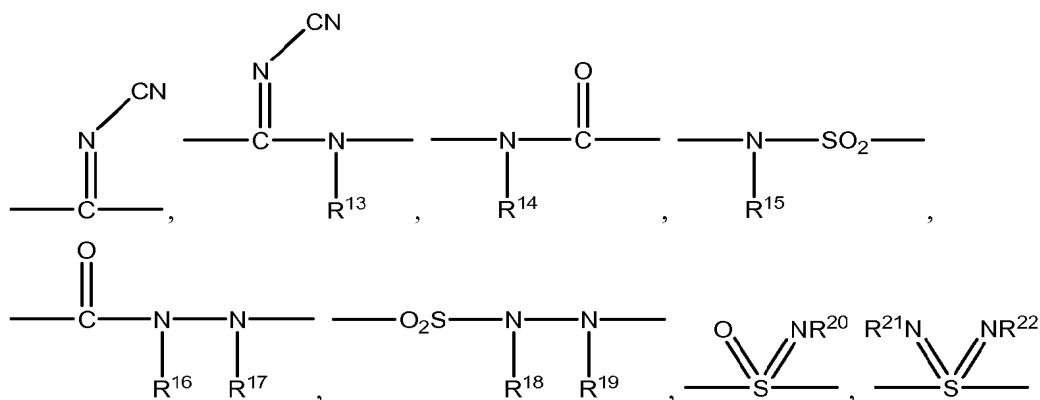
wherein

m,n,r,s and t are 0 or 1;

p is 0, 1 or 2;

V, W and X are selected from the group consisting of oxygen, hydrogen, R¹, R² or R³;

Z and Y are selected from the group consisting of CHR⁹, SO₂, SO₃, CO, CO₂, O, NR¹⁰, SO₂ NR¹¹, CONR¹²,



or Z may be absent;

$R^6, R^7, R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, R^{20}, R^{21}, R^{22}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{32}, R^{33}, R^{34}, R^{35}, R^{36}, R^{37}$, and R^{38} are selected from the group consisting of hydrogen, lower alkyl, substituted alkyl, aryl, or substituted aryl;

R^4, R^5 are selected from the group consisting of hydrogen, halo, nitro, cyano and $U-R^{23}$; U is selected from the group consisting of sulfur, oxygen, NR^{24} , CO, SO, SO_2 , CO_2 , $NR^{25} CO_2$, $NR^{26} CONR^{27}$, $NR^{28} SO_2$, $NR^{29} SO_2 NR^{30}$, $SO_2 NR^{31}$, $NR^{32} CO$, $CONR^{33}$, $PO_2 R^{34}$ and $PO_3 R^{35}$ or U is absent;

R^1, R^2 , and R^3 are selected from the group consisting of hydrogen, alkyl, alkoxy carbonyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, cyano, carboxy, carbamyl (e.g. $CONH_2$) or substituted carbamyl further selected from $CONH$ alkyl, $CONH$ aryl, $CONH$ aralkyl or cases where there are two substituents on the nitrogen selected from alkyl, aryl or aralkyl; R^8 and R^{23} are selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo;

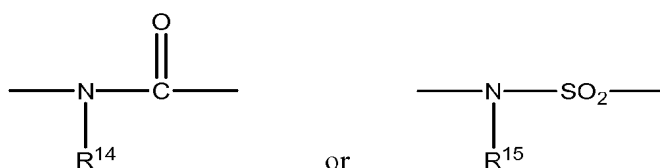
any two of R^1, R^2 , and R^3 can be joined to form a cycloalkyl group;

R, S and T are selected from the group consisting of CH_2 , CO and $CH(CH_2)_pQ$ wherein Q is $NR^{36} R^{37}$, OR^{38} , or CN; and

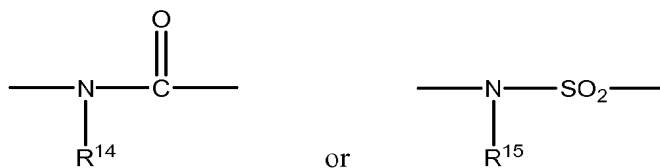
A, B, C and D are carbon, oxygen, sulfur or nitrogen.

with the provisos that

1. When m is zero then V and W are not both oxygen or
- 2 W and X together can be oxygen only if Z is either absent, O, NR^{10} , CHR^9 ,

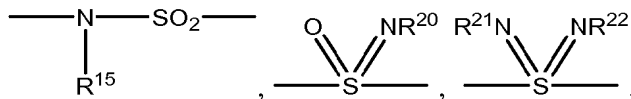


in formulas I and II, and V and X together can be oxygen only if Y is O, NR¹⁰, CHR⁹,

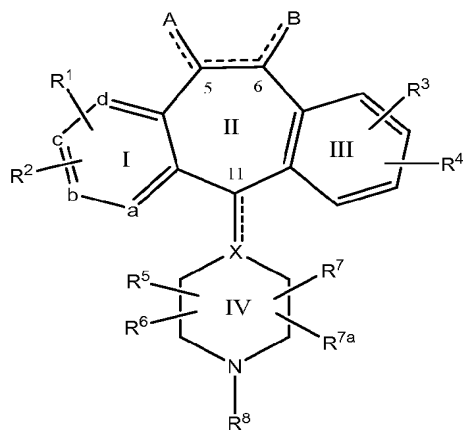


in formulas III and IV or 3. R²³ may be hydrogen except when U is SO, SO₂, NR²⁵ CO₂ or NR²⁸ SO₂, or

4. R⁸ may be hydrogen except when Z is SO₂, CO₂, or



195. A method of treating a subject with a lysosomal storage disease, the method comprising, administering to a subject with a lysosomal storage disease a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount, wherein

one of a, b, c and d represents N or N⁺O⁻, and the remaining a, b, c, and d groups represent carbon, wherein each carbon has an R¹ or R² group bound to said carbon; or

each of a, b, c, and d is carbon, wherein each carbon has an R¹ or R² group bound to said carbon;

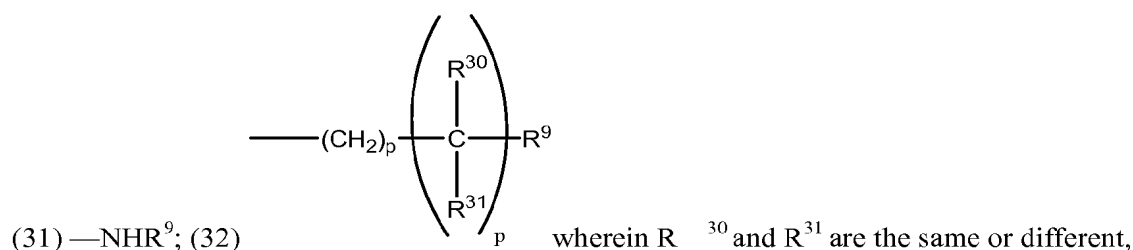
the dotted line (---) represents optional bonds;

X represents N or CH when the optional bond to C11 is absent, and represents C when the optional bond to C11 is present;

when the optional bond is present between carbon atom 5 and carbon atom 6 then there is only one A substituent bound to C-5 and there is only one B substituent bound to C-6 and A or B is other than H;

when the optional bond is not present between carbon atom 5 and carbon atom 6 then there are two A substituents bound to C-5, wherein each A substituent is independently selected, and two B substituents bound to C-6, wherein each B substituent is independently selected, and wherein at least one of the two A substituents or one of the two B substituents are H, and wherein at least one of the two A substituents or one of the two B substituents is other than H;

A and B are independently selected from the group consisting of: (1) H; (2) —R^9 ; (3) $\text{—R}^9\text{—C(O)—R}^9$; (4) $\text{—R}^9\text{—CO}_2\text{—R}^{9a}$; (5) $\text{—(CH}_2\text{)}_p\text{R}^{26}$; (6) $\text{—C(O)N(R}^9\text{)}_2$, wherein each R^9 is the same or different; (7) —C(O)NHR^9 ; (8) $\text{—C(O)NH—CH}_2\text{—C(O)—NH}_2$; (9) —C(O)NHR^{26} ; (10) $\text{—(CH}_2\text{)}_p\text{C(R}^9\text{)—O—R}^{9a}$; (11) $\text{—(CH}_2\text{)}_p\text{(R}^9\text{)}_2$, wherein each R^9 is the same or different; (12) $\text{—(CH}_2\text{)}_p\text{C(O)R}^9$; (13) $\text{—(CH}_2\text{)}_p\text{C(O)R}^{27}$; (14) $\text{—(CH}_2\text{)}_p\text{C(O)N(R}^9\text{)}_2$, wherein each R^9 is the same or different; (15) $\text{—(CH}_2\text{)}_p\text{C(O)NH(R}^9\text{)}$; (16) $\text{—(CH}_2\text{)}_p\text{C(O)N(R}^{26}\text{)}_2$, wherein each R^{26} is the same or different; (17) $\text{—(CH}_2\text{)}_p\text{N(R}^9\text{)—R}^{9a}$; (18) $\text{—(CH}_2\text{)}_p\text{N(R}^{26}\text{)}_2$, wherein R^{26} is the same or different; (19) $\text{—(CH}_2\text{)}_p\text{NHC(O)R}^5$; (20) $\text{—(CH}_2\text{)}_p\text{NHC(O)}_2\text{R}^{50}$; (21) $\text{—(CH}_2\text{)}_p\text{N(C(O)R}^{27a}\text{)}_2$ wherein each R^{27a} is the same or different; (22) $\text{—(CH}_2\text{)}_p\text{NR}^{51}\text{C(O)R}^{27}$; (23) $\text{—(CH}_2\text{)}_p\text{NR}^{51}\text{C(O)R}^{27}$ wherein R^{51} is not H, and R^{51} and R^{27} taken together with the atoms to which they are bound form a 5 or 6 membered heterocycloalkyl ring consisting; (24) $\text{—(CH}_2\text{)}_p\text{NR}^{51}\text{C(O)NR}^{27}$; (25) $\text{—(CH}_2\text{)}_p\text{NR}^{51}\text{C(O)NR}^{27}$ wherein R^{51} is not H, and R^{51} and R^{27} taken together with the atoms to which they are bound form a 5 or 6 membered heterocycloalkyl ring; (26) $\text{—(CH}_2\text{)}_p\text{NR}^{51}\text{C(O)N(R}^{27a}\text{)}_2$, wherein each R^{27a} is the same or different; (27) $\text{—(CH}_2\text{)}_p\text{NHSO}_2\text{N(R}^{51}\text{)}_2$, wherein each R^{51} is the same or different; (28) $\text{—(CH}_2\text{)}_p\text{NHCO}_2\text{R}^{50}$; (29) $\text{—(CH}_2\text{)}_p\text{NC(O)NHR}^{51}$; (30) $\text{—(CH}_2\text{)}_p\text{CO}_2\text{R}^{51}$;

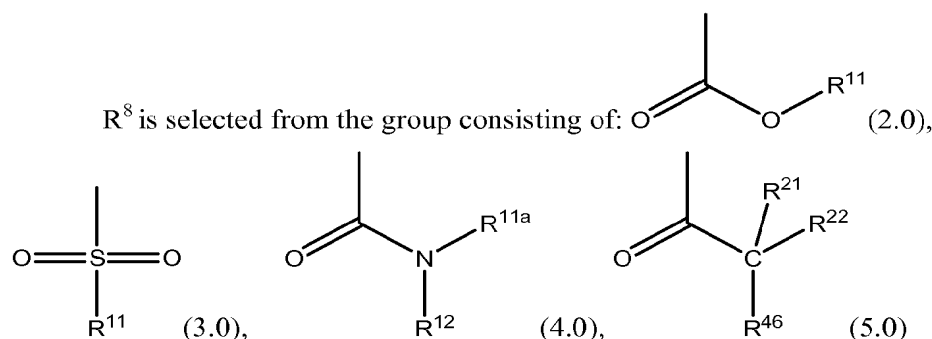


wherein R^{30} , R^{31} , R^{32} and R^{33} are the same or different; (34)-alkenyl- CO_2R^{9a} ; (35)-alkenyl- $\text{C}(\text{O})\text{R}^{9a}$; (36)-alkenyl- CO_2R^{51} ; (37)-alkenyl- $\text{C}(\text{O})\text{---}\text{R}^{27a}$; (38) $(\text{CH}_2)_p$ -alkenyl- $\text{CO}_2\text{---}\text{R}^{51}$; (39) $\text{---}(\text{CH}_2)_p\text{C}=\text{NOR}^{51}$; and (39) $\text{---}(\text{CH}_2)_p$ -phthalimid;
 p is 0, 1, 2, 3 or 4;

each R^1 and R^2 is independently selected from the group consisting of: (1) H; (2) Halo; (3) $\text{---}\text{CF}_3$; (4) $\text{---}\text{OR}^{10}$; (5) $\text{---}\text{COR}^{10}$; (6) $\text{---}\text{SR}^{10}$; (7) $\text{---}\text{S}(\text{O})_t\text{R}^{15}$ wherein t is 0, 1 or 2; (8) $\text{---}\text{N}(\text{R}^{10})_2$; (9) $\text{---}\text{NO}_2$; (10) $\text{---}\text{OC}(\text{O})\text{R}^{10}$; (11) $\text{---}\text{CO}_2\text{R}^{10}$; (12) $\text{---}\text{OCO}_2\text{R}^{15}$; (13) $\text{---}\text{CN}$; (14) $\text{---}\text{NR}^{10}\text{COOR}^{15}$; (15) $\text{---}\text{SR}^{15}\text{C}(\text{O})\text{OR}^{15}$; (16) $\text{---}\text{SR}^{15}\text{N}(\text{R}^{13})_2$ provided that R^{15} in $\text{---}\text{SR}^{15}\text{N}(\text{R}^{13})_2$ is not $\text{---}\text{CH}_2$ and wherein each R is independently selected from the group consisting of: H and $\text{---}\text{C}(\text{O})\text{OR}^{15}$; (17) benzotriazol-1-yloxy; (18) tetrazol-5-ylthio; (19) substituted tetrazol-5-ylthio; (20) alkynyl; (21) alkenyl; and (22) alkyl, said alkyl or alkenyl group optionally being substituted with halogen, $\text{---}\text{OR}^{10}$ or $\text{---}\text{CO}_2\text{R}^{10}$;

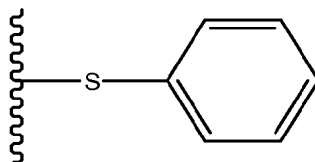
R^3 and R^4 are the same or different and each independently represent H, and any of the substituents of R^1 and R^2 ;

R^5 , R^6 , R^7 and R^{7a} each independently represent: H, $\text{---}\text{CF}_3$, $\text{---}\text{COR}^{10}$, alkyl or aryl, said alkyl or aryl optionally being substituted with $\text{---}\text{S}(\text{O})_t\text{R}^{15}$, $\text{---}\text{NR}^{10}\text{COOR}^{15}$, $\text{---}\text{C}(\text{O})\text{R}^{10}$; or $\text{---}\text{CO}_2\text{R}^{10}$, or R^5 is combined with R^6 to represent $=\text{O}$ or $=\text{S}$;



R^9 is selected from the group consisting of: (1) unsubstituted heteroaryl; (2) substituted heteroaryl; (3) arylalkoxy; (4) substituted arylalkoxy; (5) heterocycloalkyl; (6) substituted heterocycloalkyl; (7) heterocycloalkylalkyl; (8) substituted heterocycloalkylalkyl; (9) unsubstituted heteroarylalkyl; (10) substituted heteroarylalkyl; (11) unsubstituted heteroarylalkenyl; (12) substituted heteroarylalkenyl; (13) unsubstituted heteroarylalkynyl and (14) substituted heteroarylalkynyl;

wherein said substituted R^9 groups are substituted with one or more substituents selected from the group consisting of: (1) $-\text{OH}$; (2) $-\text{CO}_2R^{14}$; (3) $-\text{CH}_2\text{OR}^{14}$; (4) halogen; (5) alkyl; (6) amino; (7) trityl; (8) heterocycloalkyl; (9) cycloalkyl; (10) arylalkyl; (11)



heteroaryl; (12) heteroarylalkyl and

wherein R^{14} is independently selected from the group consisting of: H; alkyl; aryl, arylalkyl, heteroaryl and heteroarylalkyl;

R^{9a} is selected from the group consisting of: alky and arylalkyl;

R^{10} is selected from the group consisting of: H; alkyl; aryl and arylalkyl;

R^{11} is selected from the group consisting of: (1) alkyl; (2) substituted alkyl; (3) unsubstituted aryl; (4) substituted aryl; (5) unsubstituted cycloalkyl; (6) substituted cycloalkyl; (7) unsubstituted heteroaryl; (8) substituted heteroaryl; (9) heterocycloalkyl; and (10) substituted heterocycloalkyl; wherein said substituted alkyl, substituted cycloalkyl, and substituted heterocycloalkyl R^{11} groups are substituted with one or more substituents selected from the group consisting of: (1) $-\text{OH}$; (2) fluoro; and (3) alkyl; and wherein said substituted aryl and substituted heteroaryl R^{11} groups are substituted with one or more substituents independently selected from the group consisting of: (1) $-\text{OH}$; (2) halogen; and (3) alkyl;

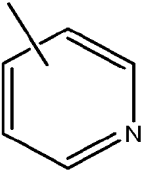
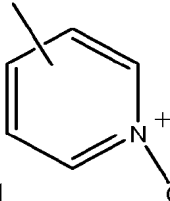
R^{11a} is selected from the group consisting of: (1) H; (2) OH; (3) alkyl; (4) substituted alkyl; (5) unsubstituted aryl; (6) substituted aryl; (7) unsubstituted cycloalkyl; (8) substituted cycloalkyl; (9) unsubstituted heteroaryl; (10) substituted heteroaryl; (11) heterocycloalkyl; and (12) substituted heterocycloalkyl; wherein said substituted alkyl, substituted cycloalkyl, and substituted heterocycloalkyl R^{11a} groups are substituted with one or more substituents independently selected from the group consisting of: (1) $-\text{OH}$; (2) $-\text{CN}$; (3) $-\text{CF}_3$; (4)

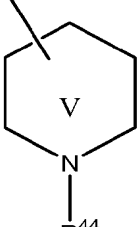
fluoro; (5) alkyl; (6) cycloalkyl; (7) heterocycloalkyl; (8) arylalkyl; (9) heteroarylalkyl; (10) alkenyl and (11) heteroalkenyl; and wherein said substituted aryl and substituted heteroaryl R^{11a} groups have one or more substituents independently selected from the group consisting of: (1) $-\text{OH}$; (2) $-\text{CN}$; (3) $-\text{CF}_3$; (4) halogen; (5) alkyl; (6) cycloalkyl; (7) heterocycloalkyl; (8) arylalkyl; (9) heteroarylalkyl; (10) alkenyl; and (11) heteroalkenyl;

R^{12} is selected from the group consisting of: H, alkyl, piperidine Ring V, cycloalkyl, and -alkyl-(piperidine Ring V);

R^{15} is selected from the group consisting of: alkyl and aryl;

R^{21} , R^{22} and R^{46} are independently selected from the group consisting of: (1) $-\text{H}$; (2) alkyl; (3) unsubstituted aryl; (4) substituted aryl substituted with one or more substituents independently selected from the group consisting of: alkyl, halogen, CF_3 and OH ; (5) unsubstituted cycloalkyl; (6) substituted cycloalkyl substituted with one or more substituents independently selected from the group consisting of: alkyl, halogen, CF_3 and OH ; (7)

heteroaryl of the formula,  and  O^- and (8) heterocycloalkyl of

the formula:  wherein R^{44} is selected from the group consisting of: (a) $-\text{H}$, (b) alkyl; (c) alkylcarbonyl; (d) alkyloxy carbonyl; (e) haloalkyl; and (f) $-\text{C}(\text{O})\text{NH}(\text{R}^{51})$;

R^{26} is selected from the group consisting of: (1) H; (2) alkyl; (3) alkoxy; (4) $-\text{CH}_2-\text{CN}$; (5) R^9 ; (6) $-\text{CH}_2\text{CO}_2\text{H}$; (7) $-\text{C}(\text{O})\text{alkyl}$; and (8) $\text{CH}_2\text{CO}_2\text{alkyl}$;

R^{27} is selected from the group consisting of: (1) $-\text{H}$; (2) $-\text{OH}$; (3) alkyl; and (4) alkoxy;

R^{27a} is selected from the group consisting of: (1) alkyl; and (2) alkoxy;

R^{30} , R^{31} , R^{32} and R^{33} are independently selected from the group consisting of: (1) $-\text{H}$; (2) $-\text{OH}$; (3) $=\text{O}$; (4) alkyl; (5) aryl (e.g. phenyl); (6) arylalkyl (e.g. benzyl); (7) $-\text{OR}^{9a}$; (8) $-\text{NH}_2$; (9) $-\text{NHR}^{9a}$; and (10) $-\text{N}(\text{R}^{9a})_2$ wherein each R^{9a} is independently selected;

R^{50} is selected from the group consisting of: (1) alkyl; (2) unsubstituted heteroaryl; (3) substituted heteroaryl; and (4) amino; wherein said substituents on said substituted R^{50} groups are independently selected from the group consisting of: alkyl, halogen, and $-\text{OH}$;

R^{51} is selected from the group consisting of: H, and alkyl;

provided that a ring carbon atom adjacent to a ring heteroatom in a substituted heterocycloalkyl moiety is not substituted with a heteroatom or a halo atom; and

provided that a ring carbon atom, that is not adjacent to a ring heteroatom, in a substituted heterocycloalkyl moiety, is not substituted with more than one heteroatom; and

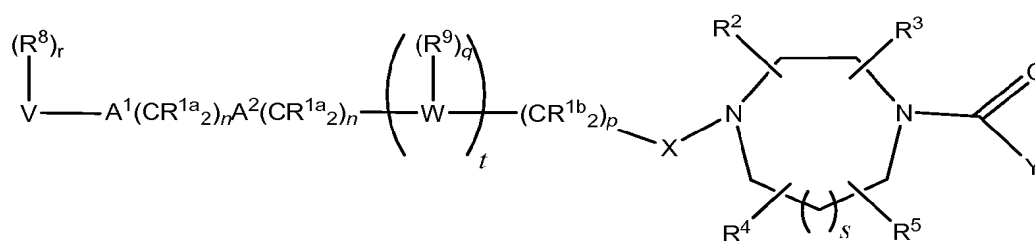
provided that a ring carbon atom, that is not adjacent to a ring heteroatom, in a substituted heterocycloalkyl moiety, is not substituted with a heteroatom and a halo atom; and

provided that a ring carbon in a substituted cycloalkyl moiety is not substituted with more than one heteroatom; and

provided that a carbon atom in a substituted alkyl moiety is not substituted with more than one heteroatom; and

provided that the same carbon atom in a substituted alkyl moiety is not substituted with both heteroatoms and halo atoms.

196. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject with a lysosomal storage disease a farnesyl transferase inhibitor compound of the formula:



or a stereoisomeric form, or a pharmaceutically acceptable acid or base addition salt form thereof, in a therapeutically effective amount,

wherein:

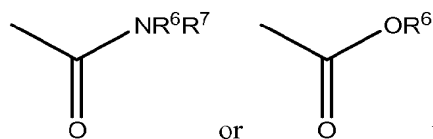
R^{1a} and R^{1b} are independently selected from:

a) hydrogen,

b) aryl, heterocycle, C_3 - C_{10} cycloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, R^{10} O-, R^{11} S(O)_m-, R^{10} C(O)NR¹⁰-, (R^{10})₂ N-C(O)-, CN, NO₂, (R^{10})₂ N-C(NR¹⁰)-, R^{10} C(O)-, R^{10} OC(O)-, N₃-, -N(R^{10})₂, or R^{11} OC(O)NR¹⁰-,

c) unsubstituted or substituted C_1 - C_6 alkyl wherein the substituent on the substituted C_1 - C_6 alkyl is selected from unsubstituted or substituted aryl, heterocyclic, C_3 - C_{10} cycloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, R^{10} O-, R^{11} S(O)_m -, R^{10} C(O)NR¹⁰ -, (R¹⁰)₂ N-C(O) -, CN, (R¹⁰)₂ N-C(NR¹⁰)-, R^{10} C(O)-, R^{10} OC(O)-, N₃, -N(R¹⁰)₂, and R^{11} OC(O)-NR¹⁰ -;

R^2 and R^3 are independently selected from: H; unsubstituted or substituted C_{1-8} alkyl, unsubstituted or substituted C_{2-8} alkenyl, unsubstituted or substituted C_{2-8} alkynyl, unsubstituted or substituted aryl, unsubstituted or substituted heterocycle,

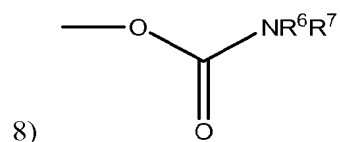
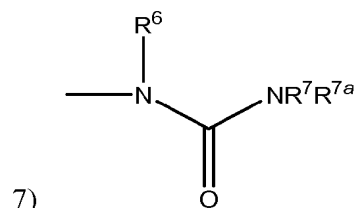
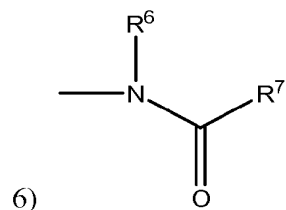


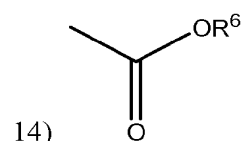
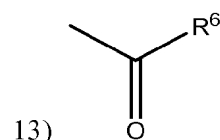
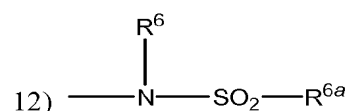
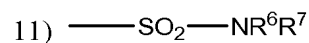
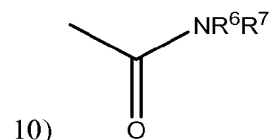
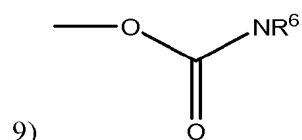
wherein the substituted group is substituted with one

or more of: 1) aryl or heterocycl, unsubstituted or substituted with:

- a) C_{1-4} alkyl,
- b) $(CH_2)_p$ OR⁶,
- c) $(CH_2)_p$ NR⁶ R⁷,
- d) halogen,
- e) CN,

- 2) C_{3-6} cycloalkyl,
- 3) OR⁶,
- 4) SR^{6a}, S(O)R^{6a}, SO₂ R^{6a},
- 5) -NR⁶R⁷,





15) N₃ or

16) F; or

R² and R³ are attached to the same C atom and are combined to form -(CH₂)_u -

wherein one of the carbon atoms is optionally replaced by a moiety selected from:

O, S(O)_m, --NC(O)--, and --N(COR¹⁰)--;

R⁴ and R⁵ are independently selected from H and CH₃ ;

and any two of R², R³, R⁴ and R⁵ are optionally attached to the same carbon atom;

R⁶, R⁷ and R^{7a} are independently selected from: H; C₁₋₄ alkyl, C₃₋₆ cycloalkyl,

heterocycle, aryl, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl,

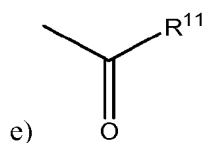
unsubstituted or substituted with:

a) C₁₋₄ alkoxy,

b) aryl or heterocycle,

c) halogen,

d) HO,



f) $-\text{SO}_2 \text{R}^{11}$, or

g) $\text{N}(\text{R}^{10})_2$; or

R^6 and R^7 may be joined in a ring;

R^7 and R^{7a} may be joined in a ring;

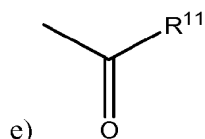
R^{6a} is selected from: C_{1-4} alkyl, C_{3-6} cycloalkyl, heterocycle, aryl, unsubstituted or substituted with:

a) C_{1-4} alkoxy,

b) aryl or heterocycle,

c) halogen,

d) HO,



f) $-\text{SO}_2 \text{R}^{11}$, or

g) $\text{N}(\text{R}^{10})_2$;

R^8 is independently selected from:

a) hydrogen,

b) aryl, heterocycle, C_3 - C_{10} cycloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, perfluoroalkyl, F, Cl, Br, $\text{R}^{10} \text{O}-$, $\text{R}^{11} \text{S}(\text{O})_m-$, $\text{R}^{10} \text{C}(\text{O})\text{NR}^{10}-$, $(\text{R}^{10})_2 \text{NC}(\text{O})-$, $\text{R}^{10}_2 \text{N}-\text{C}(\text{NR}^{10})-$, CN, NO_2 , $\text{R}^{10} \text{C}(\text{O})-$, $\text{R}^{10} \text{OC}(\text{O})-$, N_3 , $-\text{N}(\text{R}^{10})_2$, or $\text{R}^{11} \text{OC}(\text{O})\text{NR}^{10}-$, and

c) C_1 - C_6 alkyl unsubstituted or substituted by aryl, cyanophenyl, heterocycle, C_3 - C_{10} cycloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, perfluoroalkyl, F, Cl, Br, $\text{R}^{10} \text{O}-$, $\text{R}^{11} \text{S}(\text{O})_m-$, $\text{R}^{10} \text{C}(\text{O})\text{NH}-$, $(\text{R}^{10})_2 \text{NC}(\text{O})-$, $\text{R}^{10}_2 \text{N}-\text{C}(\text{NR}^{10})-$, CN, $\text{R}^{10} \text{C}(\text{O})-$, $\text{R}^{10} \text{OC}(\text{O})-$, N_3 , $-\text{N}(\text{R}^{10})_2$, or $\text{R}^{10} \text{C}(\text{O})\text{NH}-$;

R^9 is selected from:

a) hydrogen,

b) C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, perfluoroalkyl, F, Cl, Br, $\text{R}^{10} \text{O}-$, $\text{R}^{11} \text{S}(\text{O})_m-$, $\text{R}^{10} \text{C}(\text{O})\text{NR}^{10}-$, $(\text{R}^{10})_2 \text{NC}(\text{O})-$, $\text{R}^{10}_2 \text{N}-\text{C}(\text{NR}^{10})-$, CN, NO_2 , $\text{R}^{10} \text{C}(\text{O})-$, $\text{R}^{10} \text{OC}(\text{O})-$, N_3 , $-\text{N}(\text{R}^{10})_2$, or $\text{R}^{11} \text{OC}(\text{O})\text{NR}^{10}-$, and

c) C_1 - C_6 alkyl unsubstituted or substituted by perfluoroalkyl, F, Cl, Br, $\text{R}^{10} \text{O}-$, $\text{R}^{11} \text{S}(\text{O})_m-$, $\text{R}^{10} \text{C}(\text{O})\text{NR}^{10}-$, $(\text{R}^{10})_2 \text{NC}(\text{O})-$, $\text{R}^{10}_2 \text{N}-\text{C}(\text{NR}^{10})-$, CN, $\text{R}^{10} \text{C}(\text{O})-$, $\text{R}^{10} \text{OC}(\text{O})-$, N_3 , $-\text{N}(\text{R}^{10})_2$, or $\text{R}^{11} \text{OC}(\text{O})\text{NR}^{10}-$;

R^{10} is independently selected from hydrogen, C_1 - C_6 alkyl, benzyl and aryl;

R^{11} is independently selected from C_1 - C_6 alkyl and aryl;

A^1 and A^2 are independently selected from: a bond, $--CH=CH--$, $--C.tbd.C--$,

$-C(O)--$, $--C(O)NR^{10}-$, $--NR^{10}C(O)--$, O, $--N(R^{10})--$,

$-S(O)_2N(R^{10})--$, $--N(R^{10})S(O)_2-$, or $S(O)_m$;

V is selected from:

a) hydrogen,

b) heterocycle,

c) aryl,

d) C_1 - C_{20} alkyl wherein from 0 to 4 carbon atoms are replaced with a heteroatom selected from O, S, and N, and

e) C_2 - C_{20} alkenyl,

provided that V is not hydrogen if A^1 is $S(O)_m$ and V is not hydrogen if A^1 is a bond, n is 0 and A^2 is $S(O)_m$;

W is a heterocycle;

X is $--CH_2-$, $--C(=O)--$, or $--S(=O)_m-$;

Y is unsubstituted or substituted aryl or unsubstituted or substituted heterocycle,

wherein the substituted aryl or substituted heterocycle is substituted with one or more of:

1) C_{1-4} alkyl, unsubstituted or substituted with:

a) C_{1-4} alkoxy,

b) NR^6R^7 ,

c) C_{3-6} cycloalkyl,

d) aryl or heterocycle,

e) HO,

f) $--S(O)_mR^{6a}$, or

g) $--C(O)NR^6R^7$,

2) aryl or heterocycle,

3) halogen,

4) OR^6 ,

5) NR^6R^7 ,

6) CN,

7) NO_2 ,

8) CF_3 ;

9) $-\text{S}(\text{O})_m \text{R}^{6a}$,

10) $-\text{C}(\text{O})\text{NR}^6 \text{R}^7$, or

11) $\text{C}_3 - \text{C}_6$ cycloalkyl

m is 0, 1 or 2;

n is 0, 1, 2, 3 or 4;

p is 0, 1, 2, 3 or 4;

q is 1 or 2;

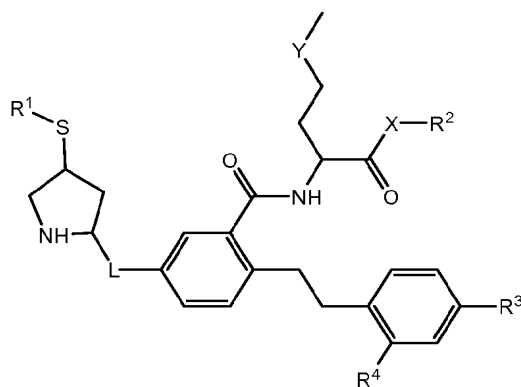
r is 0 to 5, provided that r is 0 when V is hydrogen;

s is 0 or 1;

t is 0 or 1; and

u is 4 or 5.

197. A method of treating a subject with a lysosomal storage disease, the method comprising administering to a subject with a lysosomal storage disease a therapeutically effective amount of a farnesyl transferase inhibitor of formula:



wherein

R^1 and R^2 are independently selected from H or a prodrug moiety;

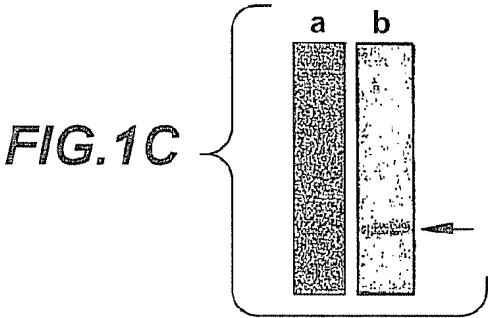
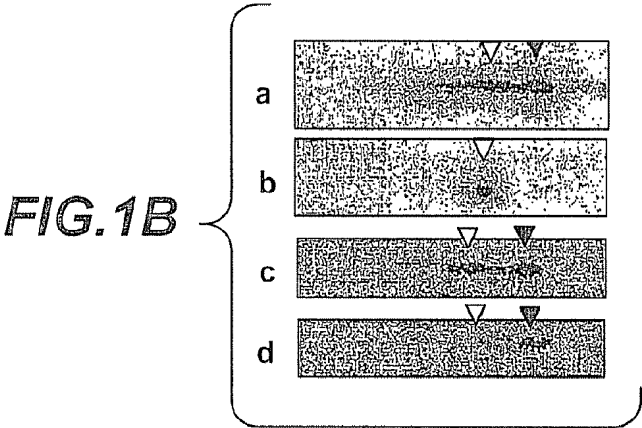
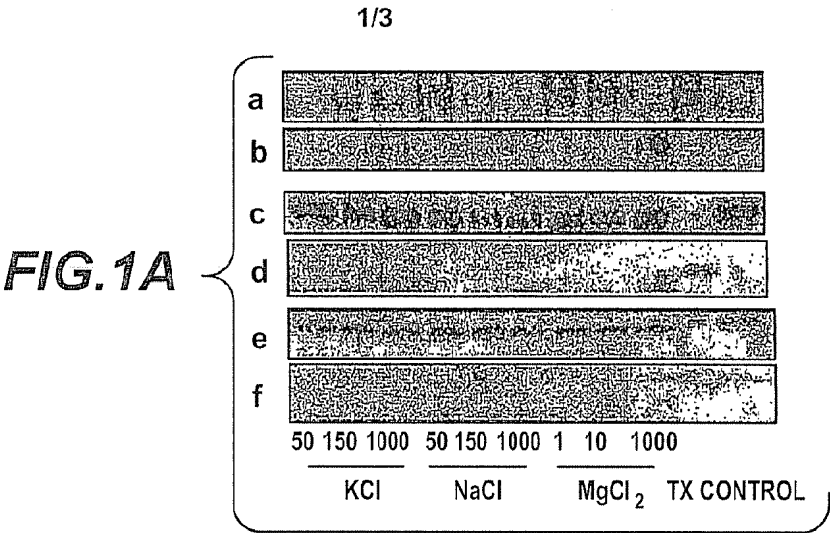
R^3 is hydrogen or halogen;

R^4 is hydrogen or halogen;

X is O or NR^2 ;

L is $-\text{CH}=\text{CH}-$ or $-\text{CH}_2-\text{Z}-$, wherein Z is NH or O;

Y is S, $\text{S}(\text{O})$, or $\text{S}(\text{O})_2$; or a derivative, analog, stereoisomer, isomer, solvate, or salt thereof.



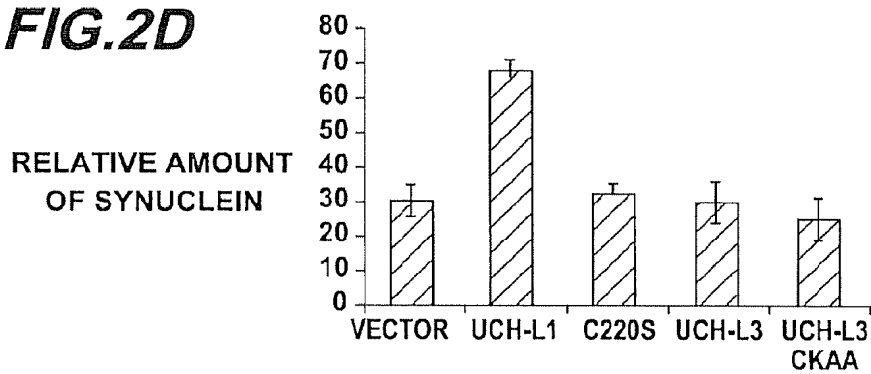
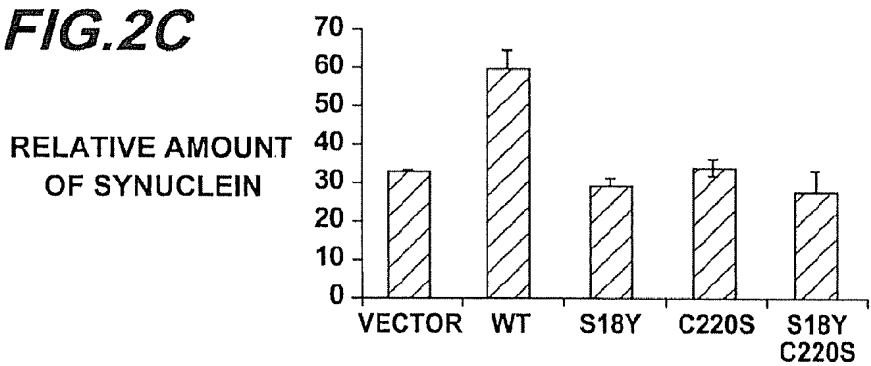
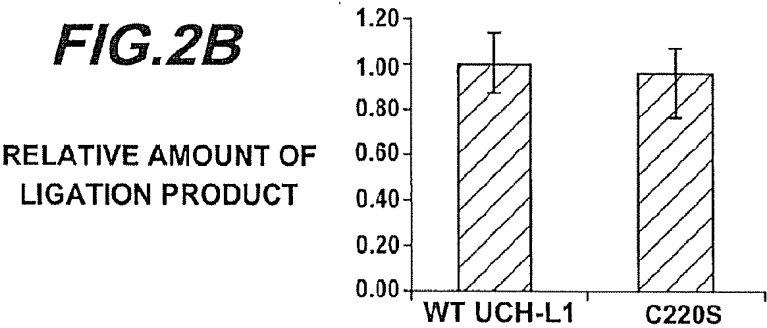
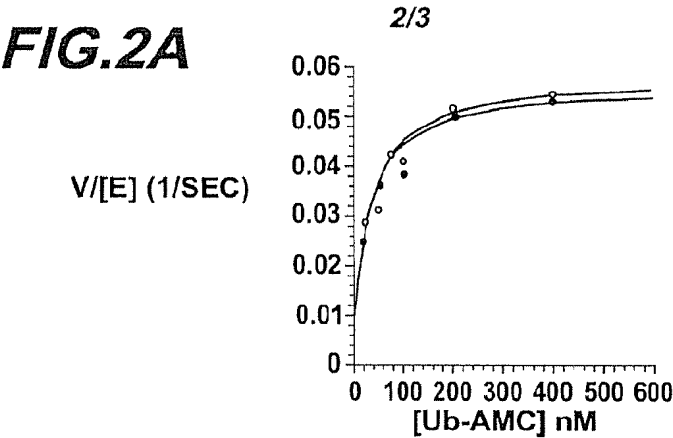


FIG.3

